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ATLAS

OF

Microscopic Diagnosis

IN

Gynecology

With Preface and Explanatory Text
by
DR. RUDOLF JOLLY, Priv. Doc.
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University of Berlin

Only authorized English Translation
by
P. W. SHEDD, M.D.
New York

WITH 52 LITHOGRAPHS IN COLOR AND 2 TEXTUAL FIGURES

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INSCRIBED
TO
MY VENERATED TEACHER
PROF. DR. MED. ROBERT OLSHAUSEN
PRIVY COUNSELLOR IN MEDICINE
WITH THE GRATITUDE OF
THE AUTHOR

PREFACE

Gynecology, nowadays, would be quite beyond comprehension without the aid of microscopic diagnosis, and the practician in diseases of women attains full growth only when he is master of the physiologic and pathologic histology of his subject. Though all its problems are, in truth, not yet solved; though many differences of opinion still exist; we have, nevertheless, a firm foundation of essentials in fact; concepts which demand and obtain universal acceptance.

Since the induction by *Olshausen* of curetment, or abrasio mucosae, as a gynecologic operation, new and, in fact, hitherto entirely unsuspected paths have opened up in diagnosis and therapy. Scraping away the mucous membrane of the uterus permits a simple, sure recognition, comparatively without danger, of the structural composition of the inner lining of this organ. Diagnosis of the benign or malignant character of mucosal alteration is determinable; a cancer is early cognized; hemorrhage, deviating from normal occurrences, is etiologically referred to an endometritis or established as an obstetric phenomenon and sequela.

Still, interpretation of the microscopic data afforded by curetage was not got in a day; only after years of tireless striving, chiefly under the leadership of *Carl Ruge*, and sequent to the determination and establishment of certain typical forms, was it possible to define more sharply the often vague lines of differentiation among the individual conditions and gather together data of the greatest import.

In later years the investigations of *Hitschmann* and *Adler* have afforded new views which, though modifying some of our earlier opinions, leave fundamentals essentially unchanged, insistent to-day, as yesterday, upon our loyal support.

Thus, in the gynecologic clinic of the University of Berlin a firmly established structural plan, a carefully defined "doctrine" of microscopic diagnosis has been gradually evolved. Numberless curetments from the University Clinic and from outside come there for microscopic examination; the line of therapeutic work to be pursued is indicated. In regular courses, the microscopic findings receive interpretation, the knowledge and experience of the lecturer communicated; and long ago the teachings, here first enunciated, became common property.

I, myself, had the good fortune to serve for a considerable period of time as assistant in the pathologic department of the gynecologic clinic, and now, again in closest touch with the practical needs of gynecologic diagnosis and teaching, have observed the lack of comprehensive and clear micro-diagnostic views. I have, therefore, bent energies to the preparation and assembling of the most important micro-representations; those, above all, of most value to the practising physician.

In Mrs. M. Ehlers was found a most excellent draughtswoman, displaying comprehensive understanding of and indefatigable industry in her work. All of the plates were prepared by her according to my specifications and are entirely accurate reproductions of microscopic preparations.

To the ever-willing responsiveness of the publishers is due the beautiful execution of the work.

BERLIN, R. JOLLY.
February, 1910.

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Microscopic Diagnosis

THE UTILITY AND TECHNIC OF MICROSCOPIC EXAMINATION

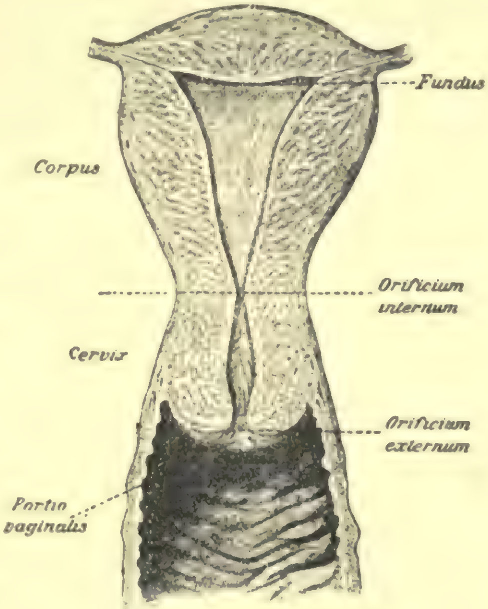
A curetment should never be looked upon as an operation of indifference. With the introduction of instruments into the uterus, infectious micro-organisms may seize the opportunity for travel; with the scraping of the wall by the sharp curet, vascular channels are easily opened, minute wounds made, through which the infection hastens. Inflammatory processes, chiefly of the parametrium, are the sequelae. Curetment, or abrasio mucosae, should, therefore, never be undertaken save where the strictest conditions of asepsis and of antisepsis prevail; the hands of the surgeon and the territory invaded are to be made ready as for an "operation," and the instruments sterilized. Moreover, this surgical interference should be limited to "clean cases," for, as a rule, it is contra-indicated where recent inflammatory processes in the small pelvis (salpingitis, parametritis) are demonstrable, as such intra-uterine invasion very possibly aggravates the conditions already present or, at least, augments the pains.

The symptom which, almost exclusively, justifies an abrasio mucosae uteri or curetment, is: hemorrhage. This may develop as menorrhagia or as metrorrhagia or, mixed with fragments of ovum and decidua, it may indicate an incomplete abortion. Recognition of an abortion offers, in most cases, no difficulty, and, this condition having been ascertained, a curetment for removal of the fetus and membranes may be done, special attention being given to all precautionary measures (large curet; care when working in the fundus; operation only in the first eight or ten weeks of pregnancy). Yet, there are hemorrhages during pregnancy, which, without further consideration, are cognized as such, *viz.*, when sequent to an abortion during the first weeks. On the other hand, after the consummation of such premature delivery longer continuing hemorrhages may be observed, due to imperfect removal of the mucous membrane or to retention of small portions of the fetal mass. In dubious cases, microscopic investigation will afford conclusions as to the origin of the abraded congeries.

Hemorrhage, furthermore, is the predominant symptom of either benign or malignant proliferations of mucous membrane, and it is in just such cases, where differentiation of the various mucosal forms and alterations is essential and practicable that, the preliminary curetage achieves its most precious results.

The uterus is a pear-shaped, musculate, hollow organ, suspended in slight anteflexioversion within the lesser pelvis. Didactically, it is divided into two parts: the *corpus*, with a cavity 4 cm. in length; the *cervix*, its canal being 3 cm. long, so that the total length of the organ is 7 cm. The walls are 1–1.5 cm. thick. The hollow of the corpus at rest in anterior, or horizontal, extension is triangular in form; in the sagittal plane, wedge shaped. Into the two superior angles or corners of the triangle empty the salpingial canals whilst the lower angle continues as the cervical canal. Both parts, corpus and cervix, are provided with a mucous membrane 1–2 mm. thick. The mucous membrane of the corpus varies from that of the cervix; the rather abrupt change is noted at the point of transition into cervical canal of the hollow of the corpus, at the so-called internal os.

The difference at this point is apparent even macroscopically, the mucous membrane of the corpus presenting a delicately undulating surface of soft, velvety consistence, while that of the cervical canal is firmer in texture and its surface arranged in more regular, arborescent (arbor vitae) rugae. The mucous membrane of the cervix ends, sharply delimited, at the os externum of the uterus. Here begins the portio vaginalis uteri, that part of the uterus projecting free into the lumen of the vagina. While the mucosa of corpus and cervix is provided with cylindric epithelia, that of the portio vaginalis, has flat cells merging in continuity with the flat epithelia of the vagina. The mucous membrane of the vagina displays more or less distinctly transverse folds, columna rugarum, which, inversely with the number of births and years, lose their virginal prominence. The macroscopically visible anatomic relativities are represented, in the above figure, in the ratio of 5:7.



Longitudinal Section of Uterus and Vagina

Consideration of the figure shows that, whatever physiologic or pathologic processes are active within the cavity of the uterine corpus, a direct examination is, ordinarily, impossible. The cervical canal, with a lumen permitting only the passage of a sound, bars, if no preparatory measures are executed, any penetration by the finger. And, even when a preliminary dilatation has been laboriously accomplished, the examining finger is able to learn only the gross anatomic changes, histologic data and values being beyond its detective ability. The curet, however, drags out the shreds of mucous membrane and starts them in the direction of a microscopic inquiry. After such fashion, opportunely, we discover carcinoma in its initial stadium and determine indications for operation. Since no other sign or symptom than the bleeding is indicative of an initial malignant alteration in the uterine mucosa as well as of an alteration entirely benign, it is ever a part of wisdom, at least in dubitable cases, to have done a microscopic examination of the products of curetment.

Malignant changes in the portio vaginalis or in the cervical canal are more accessible for digital inquiry and, ordinarily, present no diagnostic difficulties, but here, too, cases occur in which touch and vision afford no increase in knowledge. Ovula Nabothi or erosions may easily simulate a cancer; they may also serve for the genesis of a cancer. Where a case of the sort presents itself, a trial-excision in place of curetment is indicated; likewise for neoplastic changes in vagina or vulva.

Universally, the initial stadia of malignant disorders are those peculiarly difficult to recognize clinically; the advanced carcinoma is, in most cases, easily diagnosed. The essential point, however, is correct interpretation of signs and symptoms in the incipient case, while the prospects of cure by operative interference are favorable. Nor should there be hesitant fear, in these sampling curetments or excisions, that, often, the diagnosis will spell: benignity. Among the innumerable examinations made by us of the products of curetage in cases of irregular flow of blood or of excised portions where portio or vaginal wall showed tissue-change, are not a few instances of malignant degeneration in its very nascence and limited within a small area, so that the operation could be carried on in tissue entirely normal. Of the 1650 examinations of this sort made during the last three years, 147, or 9%, were malignant cases.

Hence, in the microscopic examination of the results of curetment, three morbid processes are to be borne in mind:

Abortion (products of pregnancy);
Benign mucosal change;
Malignant growths.

The technic of curetage or abrasio mucosae is as follows:

After insertion of anterior and posterior vaginal specula (*Sims'*), the anterior lip of the cervix is caught with volsellum or bullet forceps and drawn forward. To determine the direction and size of the uterine cavity, a sound is passed from the external os to the fundus. The cervical canal, in most cases not open to the passage of sounds, is dilated. The instruments best effecting this new calibration are the bent, metal dilators, which, employed in successive increase of caliber, suffice. The dilatation must be carefully and gradually accomplished, lest the cervix be torn.[9] Without an anesthetic, the dilatation, particularly at the os internum, is painful; in place of the metal instruments a thin laminaria pencil (bougie, tent) may be left in position for

12–24 hours, when the dilatation will have been more comfortably performed. It now becomes possible to introduce the curet, a rod-like instrument of nickeled copper, tipped with a moderately sharp steel spoon and easily bent to conform with the direction of the uterus. Of the various sizes of these instruments commonly at hand, one of the medium size is selected, carefully passed into the uterus to the fundus and, firmly pressed against the parieties, is withdrawn. Thus, stroke by stroke, the uterine walls are systematically scraped clean, until everywhere the instrument elicits only the sensation of steel against muscle, a sign that all mucous membrane has been removed. The extent and direction of the scraping of uterine walls required, notably of the anterior and posterior surfaces, is seen in the figure (page 5); also, the funnel-like shape of the tubal corners, where smaller instruments are needed to remove mucosal shreds otherwise beyond reach. The seizure and dragging down of the anterior lip of the cervix by forceps (volsellum, tenaculum) during curetment is necessary in hyperanteflexion and other changes of position if the cervical canal is to be kept straight. In normal position of the organ with cervix easily traversed, such traction may be dispensed with, in fact, is best dispensed with, for then, during curetment, the uterus, swung in its elastic ligaments, develops a sort of resiliency that lessens more certainly the danger of perforation.

The tissue removed by the operation is caught in a receptacle beneath, or attached to, the posterior speculum. After completing the curetage, the organ is irrigated by means of a uterine return-catheter with a hot ½–1% lysol or other disinfectant solution. Corrosive sublimate is prohibited because of its toxicity; carbolic acid solutions are to be used with caution.

Where there are suspected areas of tissue in the portio, vagina, vulva, a wedge-shaped piece is removed by knife, scissors or the excising tip of the *Paquelin* cautery. If bleeding be profuse, the wound is sewn up; ordinarily, a compress of iodoform gauze suffices.

The pieces of tissue curetted or excised are carefully washed in running water to remove the blood, so intimately mixed with them. Only when the water flows away clear are they ready for ultimate treatment; until then, the pieces of tissue are preserved in concentrated alcohol.

In the preparation of microscopic specimens, three methods are applicable:

I. Freezing;
II. Imbedding in Celloidin;
III. Imbedding in Paraffin.

The Method by Freezing

The pieces of tissue are taken from the preservative alcohol and kept in water until alcohol-free; those previously stored and hardened in formalin may be used at once. The pieces, well soaked with water, are placed upon a metal plate and sprayed with ether until the entire mass, which, during this process has been kept moist by sprinkling water upon it, is frozen to the metal. Another, and better, freezing agent is liquid carbonic acid which may be got, ready for use, in steel tanks or shells, freezing the pieces of tissue, as with ether, to the metal plate. Cutting is best done with one of the various sliding (or plane) microtomes. When the carbonic acid method is employed, a *Becker* CO_2 freezing-microtome, because of its simplicity and dependableness, is preferable to any other. The tank of carbonic acid is placed, vent below, in an iron support. The vent is connected by a flexible metal tube with the freezing-chamber, upon which the plane microtome rests. The gas tank is to be kept well distant from any source of heat (stove, furnace) and protected from the rays of the sun; otherwise an unfortunate explosion might occur. By brief openings of the vent, small quantities of the carbonic acid gas sissingly escape, until the tissue under treatment is frozen sufficiently solid for cutting; if too hard, it may be slightly moistened. The microtome is then set into action until suitable sections are cut, these being removed from the knife with a small camel's hair brush or a section-lifter and placed in water, alcohol, or, at once in the staining solution.

Imbedding in Celloidin

Celloidin is cut into small cubes, spread out in a layer and allowed to dry in air until hardened. In a mixture of alcohol and ether, equal parts, the celloidin is dissolved so that two degrees of concentration are obtained: one, easily flowing; the other of much greater density, almost viscid. The overplus of celloidin cubes must be kept from the air until used.

Before the uncut tissues are put into celloidin solutions they require preparation, as follows: Pieces that have been hardened in formalin must be soaked in running water and then placed in 75% and in 94% alcohol, 24 hours in each solution. Then, for at least 24 hours, they are left in absolute alcohol, which is changed several times, if possible. For another 24 hours, they remain in a solution of equal parts, alcohol and ether, and are then ready for immersion in the thin celloidin. Here they are kept for at least 24 hours, and, if possible, for several days, until, finally, they reach the thick celloidin and remain there for a day or two. On being taken out, the pieces of tissue are put into a shallow glass tray, thick celloidin is poured over them, and they are left to dry slowly. By covering with a glass bell and developing a more or less perfect exclusion of the air, the time of desiccation may be regulated. With completion of the imbedding, the covering of celloidin is neatly trimmed and the specimen mounted, by means of the celloidin solution, upon a microtome block. Until ready for the cutting of sections, the specimen may be kept for preservation in 75% alcohol.

The thickness of the piece of tissue for imbedding should not much exceed 0.5 cm. The imbedding of curetment material is more simple and considerably less time is required for its completion as the celloidin rapidly penetrates the small, soft shreds.

Celloidin Imbedding of Curetment Material

The shreds or pieces of tissue removed by the curet are carefully freed of blood by the use of running water, and preserved temporarily in 94% alcohol. The course of preparation for imbedding is as follows:

Absolute alcohol:	24 hours;
Ether-alcohol:	1 hour;
Thin celloidin:	3 hours;
Thick celloidin:	12 hours;
Drying.	

In using the thick celloidin, it is poured upon the tissues placed in small, open glass trays (or watch-glasses), and dried under a bell glass, which, save a slight tilting for the admission of air, covers equally one or more specimens. After desiccation, these are taken out, properly trimmed, fastened to the cutting-block, and are then ready for the microtome.

Including stain and fixation of the specimen, this method requires about 48 hours from the time of curetment to that of microscopic examination. With some practice and care, it may be done in a day, thus:

Absolute alcohol: 4–5 hours.

The alcohol must be renewed, at least, every hour, and the container shaken oftener. Continuing:

Ether-alcohol: 1 hour;
Thick celloidin: 12 hours (drying).

Omitting the "thin celloidin" period, the drying and sequent treatment follow, as above noted, with, however, the proviso that the laboratory be not too cold and damp.

The cutting of the tissue imbedded in celloidin is best done with one of the common sliding microtomes. The knife is drawn obliquely over the specimen, moistening both knife and specimen with alcohol prior to each slicing. The section is removed by placing brush or spatula beneath it, and is preserved in alcohol until its time for staining.

Imbedding in Paraffin

The pieces of tissue, as in the celloidin method, are dehydrated in absolute alcohol and then laid in xylol for some hours. They are next placed in a mixture of xylol and paraffin for 2–3 hours, followed by transfer to paraffin, melting at 50° C, and set in the paraffin oven. Here they remain for 2–5 hours, during which time the menstruum, properly, should be once renewed. After saturation with paraffin, the specimen is removed to a small box made of stiff paper (card- or bristol-board), of glass, or, of adjustable metal parts, the inner surfaces of which are brushed over with glycerin. Liquid paraffin is then poured over the tissue or tissues, and, either by immersion of the receptacle in cold water or by pouring cold water upon it, the paraffin rapidly becomes solidified. The paraffined specimen is now properly trimmed; then, fused to a permanent block or carrier of wood or other material.

Sections are then cut by one of the ordinary slide or plane microtomes with obliquely-set and dry knife and without moistening the specimen.

The sections are spread out in a dish of warm water and either are taken up, spread upon the moistened slide by a section-holder, the water removed by pressing down upon the section with blotting paper, or, the slide is slipped beneath a section, which is thus removed in position. In the incubator or over a flame, capillary attraction fastens the sections firmly to the slide. Prior to staining, the specimens are placed in xylol to remove the paraffin, then in absolute alcohol. The paraffined sections may be placed, as soon as cut, directly into xylol and absolute alcohol, but they are, as a rule, so fragile that great care must be had in handling them. Hence, it is better that they be firmly fast to the cover-glass or slide ere staining is done.

Of these three procedures in the preparation of specimens for microscopy, imbedding in celloidin is unquestionably the best for curetted material. By the paraffin method, it is doubtless possible to prepare a more durable specimen in less time, but tissue structure suffers considerably more than when imbedded in celloidin. Thus, the soft, illy-coherent mass of curetted mucous membrane is so often structurally altered by the difficultly controlled hot paraffin that diagnosis becomes impossible. Further practice permits fabrication of good specimens but the celloidin method is simpler, more dependable, easier to learn. And, it is fully adequate to the needs of gynecologic diagnosis. Sections 10–15 μ. thick are done with little difficulty, whilst specimens, necessarily thinner-cut, in the treatment of which the paraffin method is preferable, are never required.

Sections from frozen (ether, carbonic acid) material, are serviceable in many instances: for example, when quick diagnosis is desired; but, where decision is difficult, particularly in the case of curetted material, differentiation is not infrequently ill-defined and often it is impossible to cut sections adequately thin. Not rarely we have found, after preparing a frozen mount, that it was necessary to revert to the method of imbedding in celloidin for a second mount of the same specimen.

In the treatment of those tissues portrayed in the atlas of our volume, the celloidin method alone has been employed. In part, they are derived from curetment or excision, the material coming from the living patient; in part, they have been taken from the organ in its entirety or from a tumor.

The Smear

In differentiating vaginal catarrhs, the most important point to determine is whether a gonorrhea be present or not. There are not a few cases of gonococcic infection where subjective symptoms, for the most part, do not exist and where the macroscopic attributes of the secretion itself are entirely negative. Here the microscopic examination alone is decisive. And such inquiry should be undertaken in all cases where there is the slightest possibility of gonococcic infection being present. The micro-diagnostic data may include the often astounding phenomenon of an infection *in medias res.*

Yet, investigation of the vaginal secretion is far from dependable as the area and plicate surface of the part, together with the often notable quantity of its secretion, not infrequently hinder discovery of the gonococcus. More worth investigation is the urethral mucous membrane, almost invariably implicated in gonorrhea of the vagina, and in the secretion of which the gonococcus is demonstrable without difficulty. In the microscopic examination of the vaginal secretion a small portion of the exuding fluid is picked up with a flamed platinum loop and smeared or rubbed to and fro upon a clean slide. It is fixed to the glass by passing it, smear up, several times through the flame. The urethral secretion is got by pressing upon the passage from behind forward toward the symphyses until a drop appears at the orifice, which, as with the secretion from the vagina, is caught up by the platinum loop and smeared upon a slide.

Staining

For cognition of alterations in tissue, the simple nucleus-staining dyes are entirely adequate. They afford comprehensive views and accentuate the essential structural characteristics, and it is only when emphasis is desired concerning peculiarly subtile attributes that the complex stains are preferable.

In our staining of the everyday material furnished by curetments, alum-carmin is, almost exclusively, the dye employed. It has the great advantage of not overstaining and of producing a very durable specimen.

The stain is best made by heating, until it boils, 100 cm. of a 5% alum solution in a porcelain dish and then adding 1% of carmin. After 20 minutes' further heating, the solution is cooled and filtrated. This permanent solution must be refiltered prior to use in each case, a rule to be observed for all stains.

Technic of Staining

Sections that have lain in alcohol are placed for a short time in distilled water. Then in:

Alum-carmin solution, at least 10 minutes;
Rinse in distilled water;
Dehydrate in alcohol;
Clear in carbol-xylol;
Locate section on slide;
Mount in Canada balsam.

Sections may remain, uninjured, in the alum-carmin solution for a longer time, a fact of special value in tissues, as these difficultly take the dye, *e. g.* where degenerative processes have occurred.

Hemalum also gives excellent results in single color, staining deeply but paling later.

Tinction with dyes bought in solution follows the procedure noted in alum-carmin, save that the action of the solution should be briefer, 5–10 minutes.

Of double-stains, we may have hemalum or hematoxylin in combination with eosin or *van Gieson's* stain.

Eosin, which serves chiefly as contrast stain, is used in an alcoholic menstruum 1:1,000. The sections, after action of the blue stain, are again put into alcohol; after a few minutes are transferred to the eosin solution where they remain for a longer time. The rest of the procedure is identic with that of the simple hemalum stain.

Prior to using *van Gieson's* stain, the specimens, already subjected to the action of hemalum or of hematoxylin, are, carefully and for some time, washed in water. From this they are passed to a dark-red mixture of a concentrated aqueous picric acid solution and one of acid fuchsin where they remain for

3–5 minutes. After brief rinsing in water, the ordinary technic (alcohol, carbol-xylol, Canada balsam) is followed.

Staining, as a procedure which, according to the length of time and degree of concentration employed, gives most varying views, and permits differentiation of nucleus and cytoplasm, is used in malignant, degenerative processes.

Nowadays, it is deemed of great import to diagnose inflamed tissues by a demonstration of plasma cells. A procedure suited to this purpose is the *Unna - Pappenheim* methylgreen - pyronin method. The tissues must have been hardened in alcohol prior to imbedding. The preparation of sections may follow the lines of any one of the three common procedures. The sections are put into a mixture of 0.15 methylgreen, 0.25 pyronin, 20.0 glycerin, 2.5 alcohol with 100.0 parts 0.5% carbol water, remaining therein 10 minutes, or more, if necessary; then briefly de-stained in alcohol, cleared in bergamot oil, and mounted in Canada balsam. The protoplasm of the plasma cells is red, the nuclei and other tissues, green.

In staining secretions where gonorrhea is suspected, *Löffler's* methylen-blue is commendable. It is true that it does not differentiate, tinctorially, the gonococcus from other micro-organisms, but it stains the specific coccus so deeply that by form, size and location, it is easily found, if present. In staining secretions, a platinum loopful is smeared upon the slide, dried in air or flame, fixed by passing the slide (smear up) a few times through the flames, stained by a drop or two of the solution upon the smear, holding the slide 5–10 inches above the flame until slight vaporation is noted. It is then rinsed in water, dried by filter- or blotting-paper, and, covering the smear with cedar oil, the slide is brought to position under the immersion lens.

When decision is difficult, *Gram's* solution is employed. This does not stain the gonococcus but, contrarily, acts upon a great number of other bacteria. The colorless gonococcus is made visible by using *Bismarck*-brown (vesuvin) or some other dye, and thus stands out boldly in contrast with the blue, *Gram*-positive bacteria.

For further details and other stains, the reader is referred to "Pathohistologic Methods of Investigation," by *G. Schmorl* (Die pathologisch-histologischen Untersuchungsmethoden), from which some of the above data are taken.

For the microscopic observation of bacterial specimens, (the gonococcus particularly), the highest power objectives (oil immersion lens best) are required.

In the microscopic study of tissue-sections, the technic is quite otherwise, and it is needful to use the low-powered objectives. Here we begin investigation with unaided vision, then, possibly, a pocket lens—observation in general. Then, single parts are studied with the lower powers. This procedure, especially in diagnosing malignant alterations in tissue, *e. g.*, cancer alveoli, is of the greatest importance. The high powers are chiefly used in study of the tissue cell. Thus, in the atlas following, the various neoplastic forms or varieties are generalized; bird's-eye views, to use a figure. Only where details of particulate importance are under consideration, do we employ the higher objectives.

The Mucous Membrane and Epithelium of the Uterus

Plate I. Figs. 1 and 2

Plate I

Fig. 1. Mucous Membrane of the Corpus Uteri
Fig. 2. Varieties of Epithelia in the Normal Uterus

Fig. 1. The Mucous Membrane of the Corpus Uteri

Alum-carmin × 30

The mucous membrane lining the inner surface of the uterus is about 1 mm. thick. Under certain conditions, it may wrinkle, shrivel up, or, greatly increase in thickness.

It is divisible into two parts: one of connective tissue; the other, epithelial. The connective tissue, also termed stroma or interstitial tissue, is chiefly composed of round cells (so-called "stroma cells") with large nuclei that seem almost to burst their containers. These cells, capable of protean vital change in form and size, are seen under the microscope as minute red points. The structural web or net of connective tissue among the meshes of which these cells lie, becomes visible only by special stain and the higher objectives but, practically, they have no significance and hence are not depicted.

The epithelia of the mucous membrane cover the entire inner surface in a single stratum, in numerous places boring deeply into subjacent tissue and forming glands. These glands are tubular, pursue a slightly spiral or serpentine course and dip down to the base of the mucosa, sometimes continuing into the musculature. They are discretely placed, with intervals of 3–4 times their diameter; in deeper portions of the mucosa they lie nearer together. Because of the twisting course, sections present only parts of glands.

The mucosa rests directly upon the uterine muscle, there being no submucosa. The musculature consists of fascicles of smooth muscle fibers, extremely devious in course.

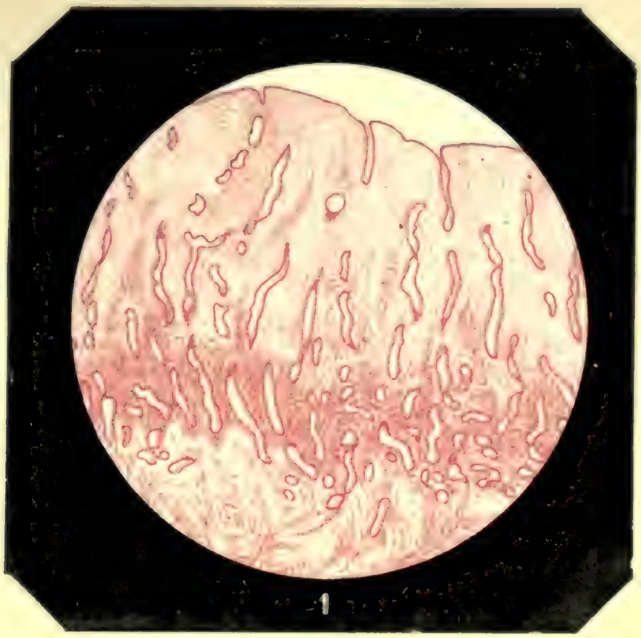


Fig. 1. Mucosa of the body of the uterus

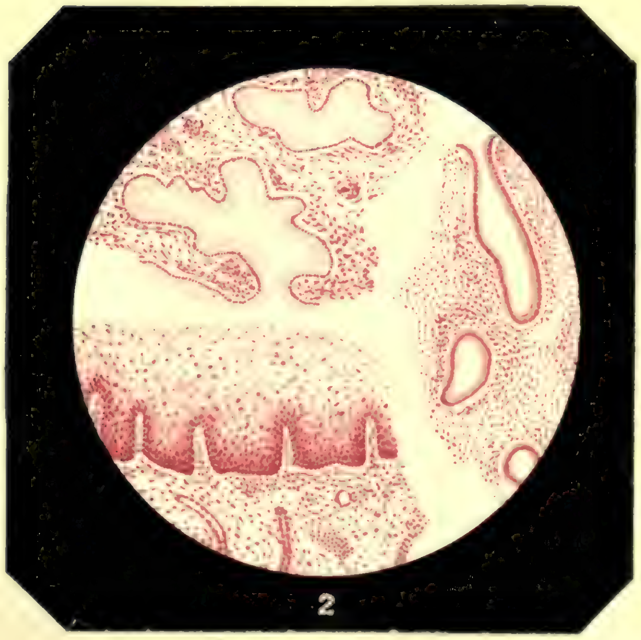


Fig. 2. Epithelia of the normal uterus

Fig. 2. The Forms of Epithelia in the Normal Uterus

Alum-carmin × 140

The epithelia of the mucous membrane of the body of the uterus consist of low cylinder cells, which both upon the superficies of uterine mucosa and in the glands, are structurally similar. They possess nuclei, approximately central and taking a dye well, and the tops or exposed surfaces of the cells are provided with cilia. The stroma cells in the vicinity of a gland are often found closer together. Figure 2 is representative of material obtained by curetage; to the right, are seen the mucous membrane of the corpus uteri and three glands, one cut longitudinally, the two others, transversely.

The epithelia of the cervix are likewise cylindric but of greater height than those of the corpus. The body of the cell is most delicate in structure; at the base is found the nucleus. The cervical glands, lined with these epithelia, are, contrary to the construction of uterine glands, acinous in type. The supporting connective tissue or stroma has fewer cells and is more rigid than that of the corpus. The upper portion of the section shows two cervical glands, one cut longitudinally, the other transversely. In the connective tissue are a few capillary blood-vessels.

Whilst these two epithelial forms at the os internum uteri are rather sharply contrasted with one another, there begins at the external orifice a transition to flat epithelia in multiple strata. The large, delicately textured cells have small, centrally-located nuclei. The base of the cell is polygonal, tending, as it approaches the surface, to lose its angularity and flatten out. At varying distances are found inversions (the so-called papillae) in the bases of these flat epithelial cells. The lower portion of the view depicts a bit of surface covered with flat epithelia, and originally located at the portio vaginalis uteri but scraped off accidentally during curetment. In subepithelial tissues some blood-vessels are seen here and there.

Endometritis

Plates II—V. Figs. 3—10

Plate II

Figs. 3 and 4. Endometritis glandularis

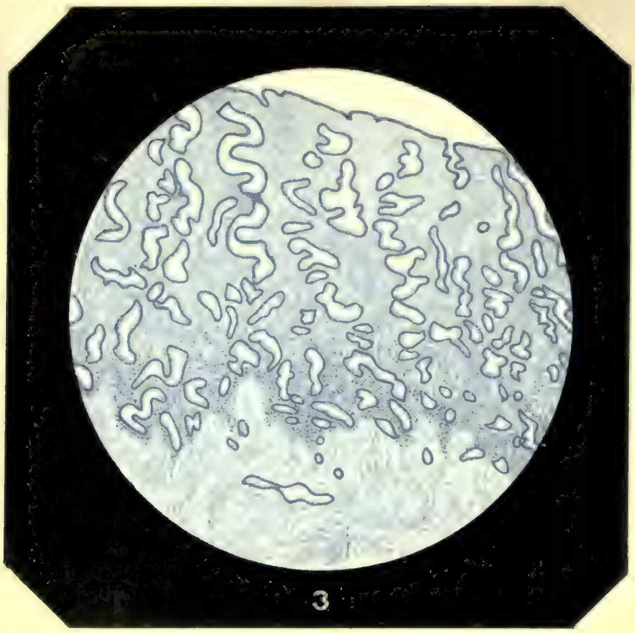


Fig. 3. Endometritis glandularis

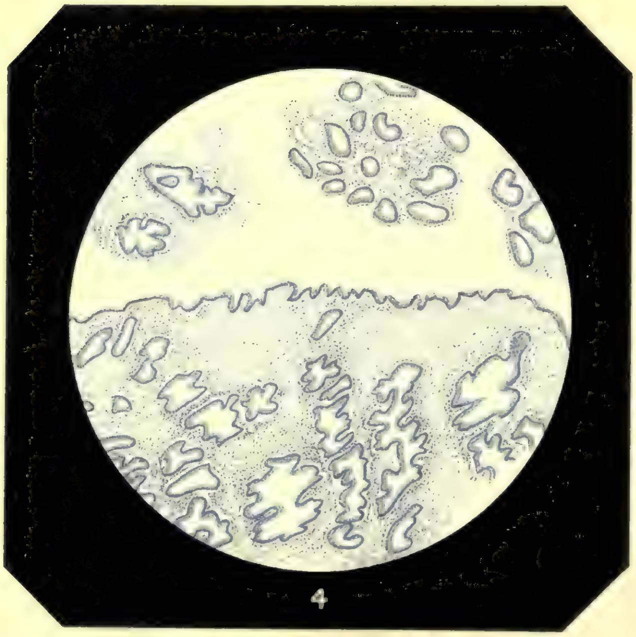


Fig. 4. Endometritis glandularis

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Fig. 3. Endometritis glandularis

Hemalum × 30.

With the concept of endometritis are linked together, quite generally, changes of tissue, of function, or both, which, essentially, depend upon augmentation of the cellular elements in mucous membranes. True or idiopathic inflammation in the patho-anatomic sense of the term is not essential. This multiplication of cellular elements in mucous membrane may be limited to glands alone: endometritis glandularis; to connective tissue exclusively: endometritis interstitialis; or to both species of cellular elements: endometritis diffusa.

The endometritis glandularis, as shown in Fig. 3. has increase in both size and number of its glands. Where glands increase, individually, in size only, the condition is termed: endometritis glandularis hypertrophica; if there is increase in the number of glands: endometritis glandularis hyperplastica. Mixed forms are common. If connective tissue does not keep pace with glandular growth, then the glands are forced to alterations in form if progress is to continue.

Fig. 4. Endometritis glandularis

Hemalum × 50

The morphologic changes in glands may develop, when endometritis glandularis is present, along odd and most variant lines. Thus, a gland may lie in coil, like a snake, while its walls are hacked, indentate. Another gland may, in its entirety, have a spiral or corkscrew form, yet also provided with irregular eversions, diverticula, or, it may be pressed together after the fashion of the musical instrument dubbed accordion.

The lower half of this view of curetment-material shows a piece of mucous membrane cut longitudinally; the upper half, three, cut obliquely. The longitudinal section with its dentate sides, and the asteroid oblique or transverse sections have a degree of resemblance to sections of glands during pregnancy, and it has been maintained that changes of this type in the morphology of glands are always associated with menstruation. This is true, in a degree, for there are many cases of this description. Such forms are often found where there is absolutely no relativity with the catamenia, and, contrariwise, the menstrual complex has often been observed where no alterations in the morphology of glands have been present. And, furthermore, the section here depicted was derived from a curetment executed between menstruations, and the concept of endometritis glandularis hypertrophica must, therefore, be considered as entirely irrelative to the menstrual epoch.

Plate III

Fig. 5. Endometritis interstitialis
Fig. 6. Endometritis atrophicans. Endometrium senile

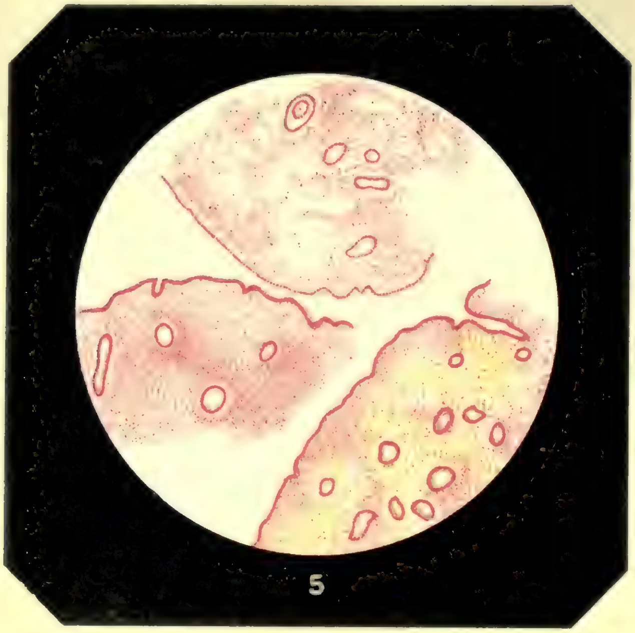

Fig. 5. Endometritis interstitialis

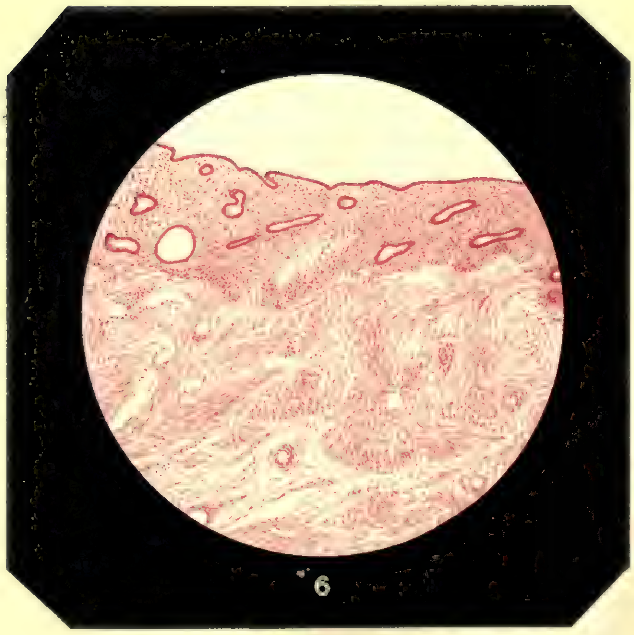

Fig. 6. Endometritis atrophicans. Endometrium senile

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Fig. 5. Endometritis interstitialis

Alum-carmin × 30

The mutations here affect chiefly the interstitial portion of the mucous membrane, notable change being visible in the number, size or form of the stroma cells. Endometritis interstitialis may be acute or chronic in type, the genesis of the chronic form being particularly evident when the connective tissue cells take on the spindle form and become more rigid and striped in texture.

The curetted material (mucosa) here depicted is in three portions, showing different forms of an acute endometritis interstitialis, in all of which the small number of glands present is noticeable.

In the upper piece are interstices in the interstitial tissue, due to exudative processes; the texture is loose in character, and we have an example of endometritis interstitialis exsudativa. Of the glands in transverse section, the uppermost shows an invagination or inversion in the direction of its long axis, so that we have one epithelial ring enclosing another.

In the lowest piece of mucous membrane, free blood is seen in the interstitial tissue; we have, therefore, endometritis interstitialis haemorrhagica.

In the middle piece the cellular elements preponderate; their number is very great, and they are close together. In these forms, special stains sometimes bring plasma cells into view.

Fig. 6. Endometritis atrophicans. Endometrium senile

Alum-carmin × 30

During the menopause, the uterus begins its retrogressent years and lessens in volume. Synchronously, the mucosa wrinkles and perceptibly thins or loses in depth. The glands, hitherto perpendicular to the mucosal plane, run awry, obliquely, as a result of the shriveling of the mucous membrane. The glands also atrophy; their normal caliber decreases, though cystic dilatation from stoppage of the mouth of the gland is occasionally seen. The connective tissue cells become slowly spindle-shaped, similar to their appearance in chronic interstitial endometritis. Comparison of our present slide with the sexually mature endometrium shown in Figure 1: is lucid differentiation.

The uterine wall also demonstrates change, the connective tissue beginning to predominate whilst musculature exhibits its own degenerative processes.

Plate IV.

Fig. 7. Endometritis diffusa fungosa
Fig. 8. Endometritis polyposa cystica

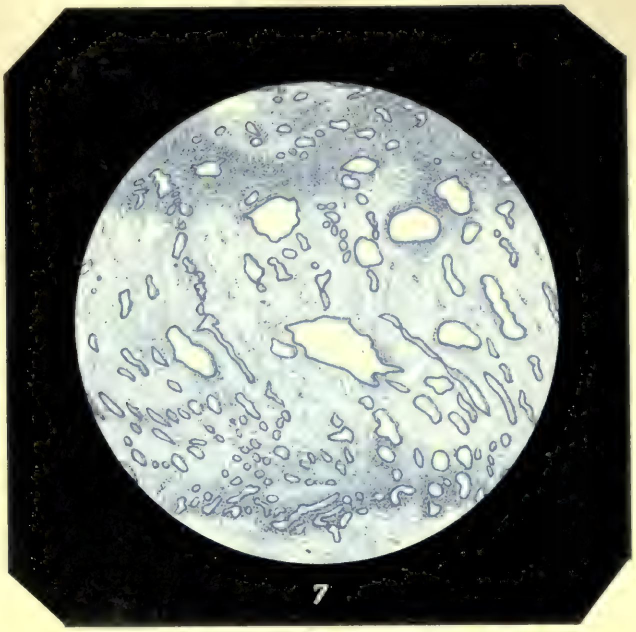

Fig. 7. Endometritis diffusa fungosa

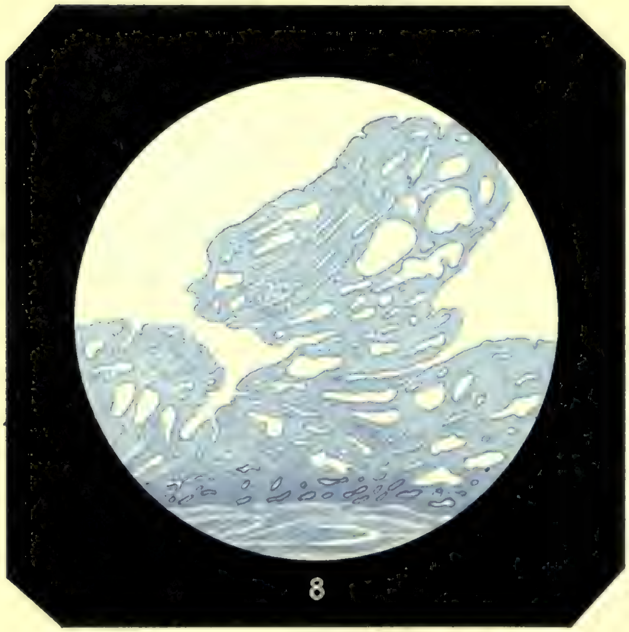

Fig. 8. Endometritis polyposa cystica

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Fig. 7. Endometritis diffusa fungosa
Hemalum × 12

"There is a chronic affection of the mucous membrane of the uterus which, though the normal cellular elements be retained, leads to fairly notable mucosal thickening (3–4 times normal). The epithelia of normal mucous membrane are found only in the glands even as these, with the exception here and there of a dilatation, remain, morphologically, unaltered. Hemorrhage, chronic and profuse, is the most important and almost the only symptom of this disease."

This definition, first introduced by *Olshausen* in the year 1875 (Archiv für Gynäkologie, Bd. 8) is now universally recognized. The morbid condition is one of increase in both the interstitial and glandular components of the mucous membrane. The affix, "fungosa," (fungus—sponge) indicates the soft, spongy texture or quality of the mucosa.

The trouble may appear in a uterus otherwise normal, as, for example, in a myomatous organ where the increased thickness of the mucous membrane is extreme (1 cm. or more). The hemorrhages occurring in uterus myomatosus, are chiefly due to this alteration in character of the mucosa. The view depicts infiltration of round cells in the greatly proliferate mucous membrane, in connective tissue. The glands are, in part, of normal type; the remainder, much dilated.

Fig. 8. Endometritis polyposa cystica

Hemalum × 5

In contrast to the condition above stated, we have irregular proliferation of the mucous membrane. Some portions rise high above the common plane and become polypous growths.

Microscopically, it is the glandular part of the mucosa that is particularly affected, the glands dilating into numerous cystic formations. In a slide of curetted material, diagnosis is established when transverse section of some pieces of tissue shows epithelia on three sides of each piece, the deduction from such premises being that, the portion of mucosa in question rose above, overtopped the common plane. In such case there would be either a single mucosal polyp or, diffuse polypous formations.

In rare instance, a single large polyp, mucosal in origin, is found in the fundus. It is difficultly cognized, for the curet does not always engage with it. Since it may, however, lead to copious uterine bleedings, the dilatation of the cervical canal and investigation of the uterine cavity digitally may be required.

In this, and the preceding view, magnification by a simple lens has been given that a generalizing concept may be had. In this way, the entire polypous formation becomes visible, and we see how its small stem rises from the mucosal surface.

Plate V.

Fig. 9. Endometritis tuberculosa
Fig. 10. Plasma cells in connective tissue

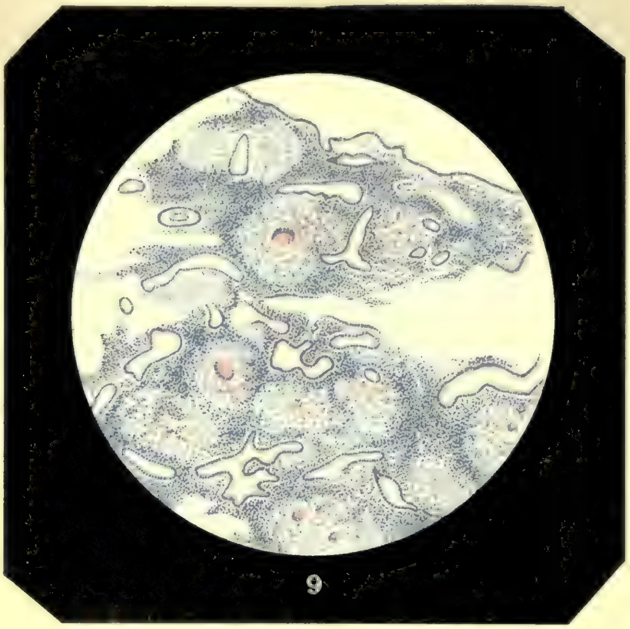

Fig. 9. Endometritis tuberculosa

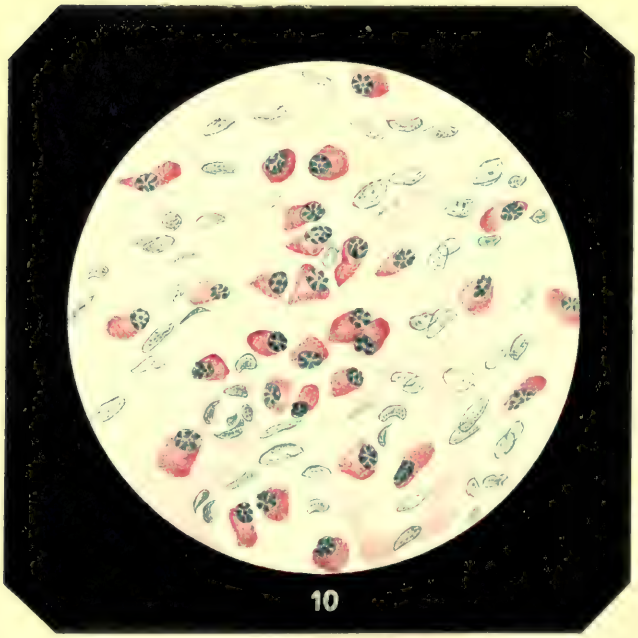

Fig. 10. Plasma cells in connective tissue

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Fig. 9. Endometritis tuberculosa

Hemalum; Eosin; × 50

While most of the benign changes in the endometrium are attributed to hypertrophic or to atrophic processes, there are also inflammations of the endometrium due to idiopathic and infectious agents. In many cases of puerperal fever, penetration of strepto- or staphylococci through mucous membrane and uterine wall has been demonstrated. Rare is the symptom-complex of a tuberculous infection found in a micro-examination of material derived from curetment.

The tubercles are found (plainly visible in the section) in interstitial tissue which they more or less destroy. In the center of the tuberculous foci, giant cells with notably distinct nuclei are disposed with some regularity. The glands in this specimen of uterine mucosa are but little affected. Demonstration of tubercle bacilli in these tissues is unnecessary as microscopic study of the tissue structure here presented permits no misinterpretation with regard to the genetic factor.

Fig. 10. Plasma cells in connective tissue

Methylgreen-pyronin (Unna-Pappenheim) × 550

Lately, there has been made emphatic and definite demand that, the term: endometritis, be used only when inflammation, in the patho-anatomic sense of the word, is present. As criterion, it is proposed that demonstration of plasma cells in connective tissue be taken and, furthermore, that connective or interstitial tissue (stroma) in particulate, be accepted as the characteristic and homesteading site of inflammation. To any morbifacient or other alterations in glandular tissues only secondary worth is to be attributed, and such changes are no more to be included in the concept and appellation: endometritis.

Despite this, I have retained the descriptive rubric originally emanating from *Carl Ruge*. In the first place, the inflammatory process in particulate is a process not yet fully elucidated, and furthermore, the origin of these plasma cells and their appearance in tissues have thus far been interpreted in fashions chiefly interesting because of their variety. Also, they have been found occasionally in healthy tissue and frequently noted as absent in inflamed tissue.

Again, the glands, in contrast to connective tissue, may present alteration so extreme that the primary morbific process must have had origin in them.

That this, however, is not always to be conceived as a simple increase in the number of cellular elements is demonstrable by the glandular forms (among other phenomena) that stand upon the border line beyond which is malignancy; forms with which stimuli, irritations are implicate, conjoined, and concerning which no elucidation has thus far been proffered.

The plasma cells depicted in the section are from the connective tissue of the portio vaginalis uteri. Their nuclei are eccentric in location; the chromatin bodies star-shaped in arrangement and green of hue; the protoplasm stained red. The staining of plasma cells is a process requiring more than ordinary practice and experience; practically, their significance approximates nil.

Erosio portionis

Plates VI and VII. Figs. 11–14

Plate VI

Fig. 11. Erosio portionis simplex
Fig. 12. Erosio portionis papillaris

Fig. 11. Erosio portionis simplex
Hemalum × 16

In conditions where chronic irritation is present, chiefly sequent to vicious uterine catarrhs, there appear at the portio vaginalis uteri scarlet-red flecks which, at first, give the impression of an actual loss of uterine substance; hence, dubbed: erosion. In truth, however, the condition is not one of loss of substance but, as demonstrated by *C. Ruge* and *J. Veit*, it is a case of substitution by cylindric epithelia for the flat epithelia normally present in this region. The nomenclature, despite this fact, has been retained, as it agrees with the clinical concept of this condition and offers contrast to the term: ulcus portionis which, being interpreted, has to do with epithelial defect.

The notable redness attained by those areas of the portio vaginalis altered by "erosion," is brought about by the substitution, for flat epithelia in several layers, of cylindric epithelia in a single stratum, underneath and through which, the scarlet mucosa of the cervix and the red tissue of the portio shimmer.

By "erosio simplex," we mean the simple substitution of cylindric for the normally present flat epithelia and the upsurging of some glands, structurally cervical, into the territories of the portio vaginalis.

The section depicts an excised area of the portio in erosio simplex. Leftward, flat epithelia are still visible but, passing to the right, we note the invasion by cylindric epithelia, shoving up and off the indigenous flat cells. Some cervical glands have already pushed forward under the flat epithelia.

Fig. 12. Erosio portionis papillaris

Hemalum × 8

The pushing hither and thither of epithelia and the proliferations of mucous membrane do not occur always within a single plane nor remain at one level, but may, opportunely, rise above the surface and erect themselves in papillous growths. Even clinical data permit, conditionally, the acquisition of this knowledge, as when the inquiring digit glides over a velvet surface and impinges upon small, bud-like formations.

Such papillary growths in the region of the portio vaginalis uteri are reproduced in our picture with the magnification (× 8) of a simple lens. To the right there is still to be seen a small area of flat epithelia; to the left, a much-dilated gland.

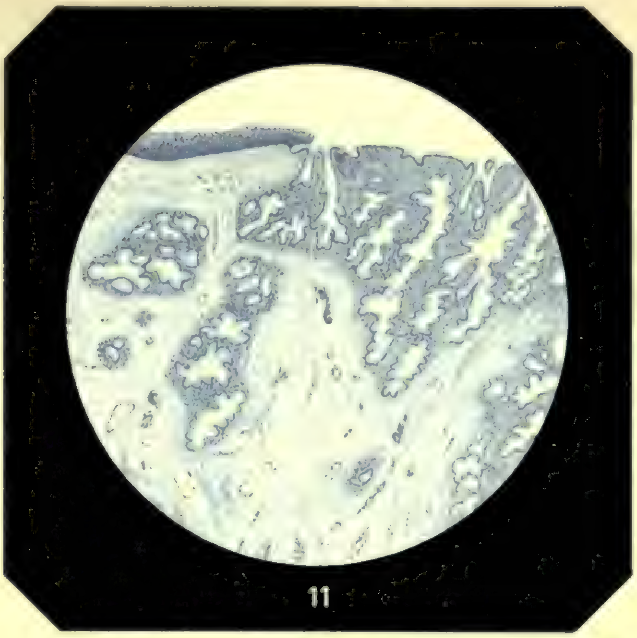

Fig. 11. Erosio portionis simplex

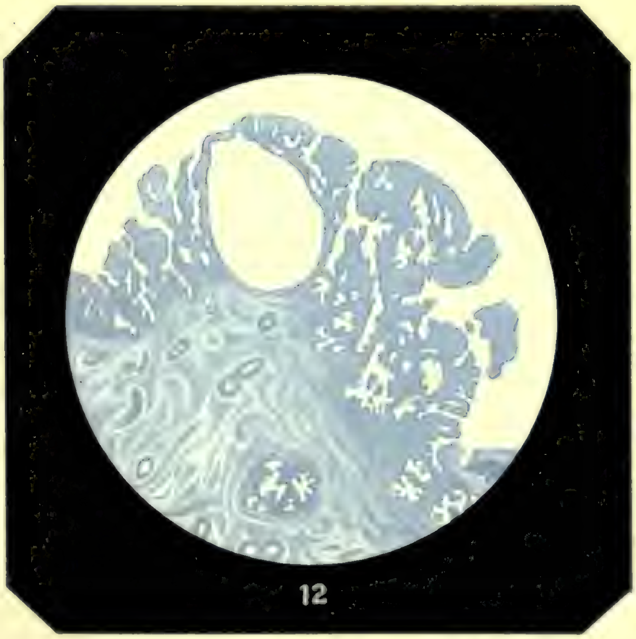

Fig. 12. Erosio portionis papillaris

Plate VII

Fig. 13. Erosio portionis glandularis

Fig. 14. Erosio portionis (healing)

Fig. 13. Erosio portionis glandularis
Alum-carmin × 8

The newborn glands within the territory of the portio vaginalis are innately capable of many transformations, the most ordinary of which is: cystic dilatation. Closure of the gland's mouth results in tsasis of secretion, in progressive circumferential increase of the gland which shoves it superiorly or toward the superficies where it finally appears as a small, hard, gray-white bud or nodule, and may thus be cognized during digital examination. These nodules, when incised, exude a vitreous mucus, a cervical gland's secretion, and are dubbed: ovula Nabothi. Dilated glands near together may become confluent by a breaking-down of adjacent parietes.

The general view of the section, afforded by the simple lenticular magnification, shows a number of these gland dilatations; at one point, an incipient ovulum Nabothi. The epithelia of the gland have been mostly destroyed by the extreme dilatation and tension. To the left in the view, is a bit of squamous epithelium not yet disintegrated.

Fig. 14. Erosio portionis (in process of healing)
Alum-carmin × 60

Erosion of that portion of the uterus protruding into the vagina may return to norm spontaneously. In such case restoration is effected by the flat epithelia advancing from the side lines toward center, growing, in part, over glands; in part, into them. In the first instance, glandular tissue is retained in the depths, permitting a future renascence of the erosion. This process, at the most a temporary cure, is called: sanatio incompleta.

In the second instance, the advancing flat epithelia lift and scatter the glandular cylindric epithelia, shoving under and gradually enucleating the gland. Finally the portio vaginalis uteri is garbed anew with normal habiliments, and we have: sanatio completa.

Often, both processes of restoration are observed in one specimen, as in the section here presented. In the large gland near the center, the advancing flat epithelia are about to split off the cylindric epithelia from the parietes of the gland and penetrate the depths, later occupying in undisputed power the territory held by the gland. In the case of other glands (to the right and left), bridges of flat epithelia have been thrown across. Within the eroded area is found a round-cell infiltration, wherein not a few plasma cells are demonstrable.

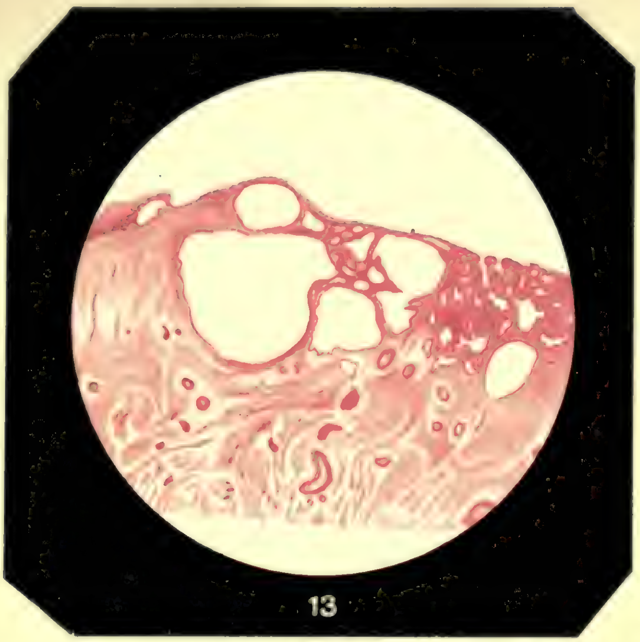

Fig. 13. Erosio portionis glandularis

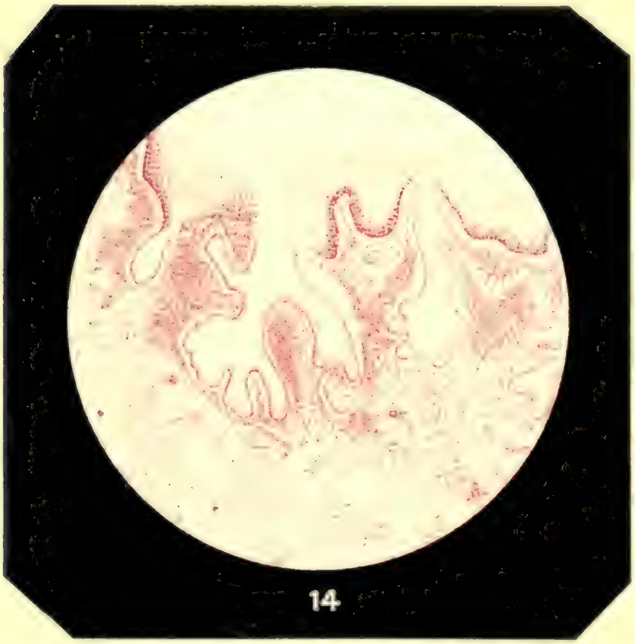

Fig. 14. Erosio portionis in process of cure

Menstruation

Plates VIII and IX. Figs. 15—18

Plate VIII

Fig. 15. Premenstrual Congestion

Fig. 16. The Blood-burst

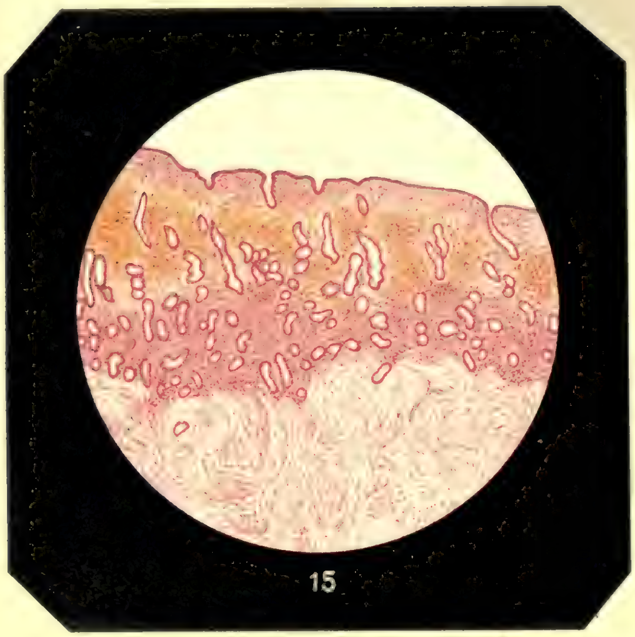

Fig. 15. Premenstrual congestion

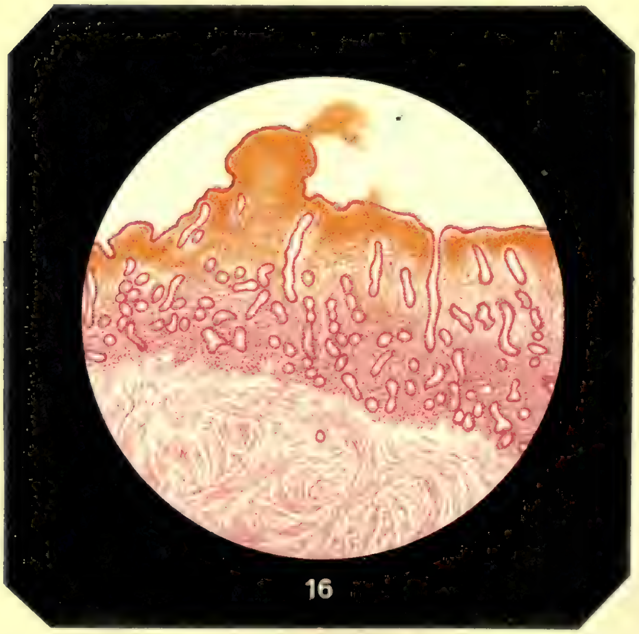

Fig. 16. Blood-burst or the menstrual hemorrhage

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Fig. 15. Premenstrual Congestion
Alum-carmin × 30

By menstruation is meant a flow of blood at regular intervals from the mature endometrium. Ovulation, the progress of ovum from ovarium,—these phenomena are in close relationship with the premenstrual congestion. In menstruation, three stages have been differentiated: (1.) Premenstrual congestion; (2.) The hematic flux; (3.) Restoration of the mucous membrane.

In the first stage, the interstitial tissue of the mucosa appears drenched with blood and exhibits looser texture, particularly when near the mucosal surface. The glands may assume forms similar to those of endometritis glandularis hypertrophica, though results of the sort are by no means constant, invariable. As shown in Figs. 15 and 16, the glandular tissue may remain unaltered.

Fig. 16. The Blood-burst
Alum-carmin × 30

The blood pushes on upward to the superficies of the mucous membrane and collects beneath the epithelia. These are raised and shattered by the pressure or the blood seeps through the cells. Because of the hemorrhage and the serous maceration of the upper portion of the mucous membrane, the glands are forced apart and thus appear scanty in number.

The microscopic view of the third stadium, *i. e.*, of the post-menstrual restoration of mucous membrane, is similar to that of the first. The blood still present in interstitial tissue is gradually resorbed and the glands, apt to be dilated at the beginning of menstruation, may appear collapsed. However, though there be actual destruction and loss of portions of the mucous membrane, it is not in anywise essential to the normal progress of the catamenia.

Plate IX

Fig. 17. Decidua menstrualis

Fig. 18. Membrana dysmenorrhoica
(Endometritis exfoliativa)

Fig. 17. Decidua Menstrualis

Alum-carmin × 30

Menstruation frequently exerts an irritant effect upon the mucous membrane, causing proliferative tendencies to develop. The glands change in form, the connective tissue cells become larger, the entire mucous membrane is elevated, and the difference between the surface and deeper parts (intimated during the intermenstrual period) is more sharply accentuated. The whole picture recalls a true decidua of pregnancy save that the degree of alteration is not as great.

Especial consideration is to be vouchsafed remarkable forms of gland tissue. Epithelia wind their way in cords, threads, into the lumen of the gland so that a gland, if cut longitudinally, has a saw-edge contour; if cut transversely, an asteroid outline. The glands also are larger and the secretion emanating from the epithelial cells is increased.

These changes begin some days before the flux; augment until the acme of the menstrual function is attained; decrease and end as norm is reached. In the period of time between two successive menstruations, the mucous membrane remains undisturbed. As the process is repeated with each catamenial epoch, the term: menstrual cycle, seems not inappropriate.

The hypothesis is fairly seducing that, the mucous membrane of menstruation regularly and physiologically develops a decidua, similar, and similarly prepared, as for the reception of an ovum. The hypothesis, however, does not agree with the fact that oftentimes menstruation finishes its course without the development of variations of the sort

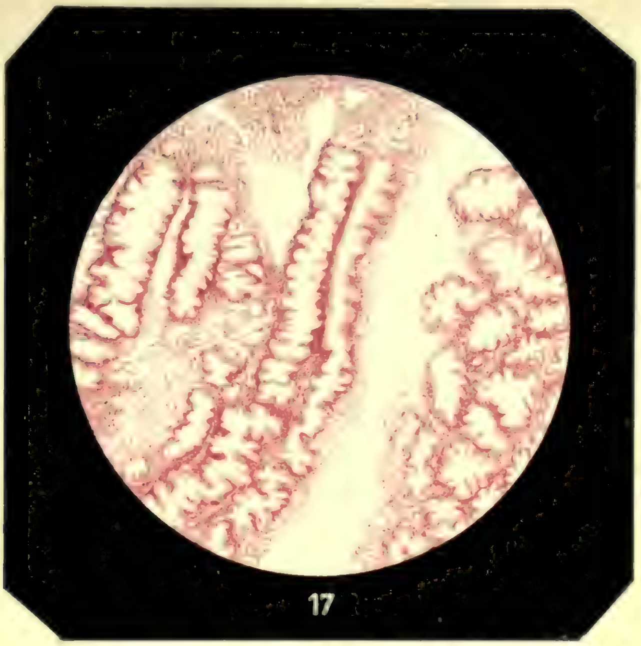

Fig. 17. Decidua menstrualis

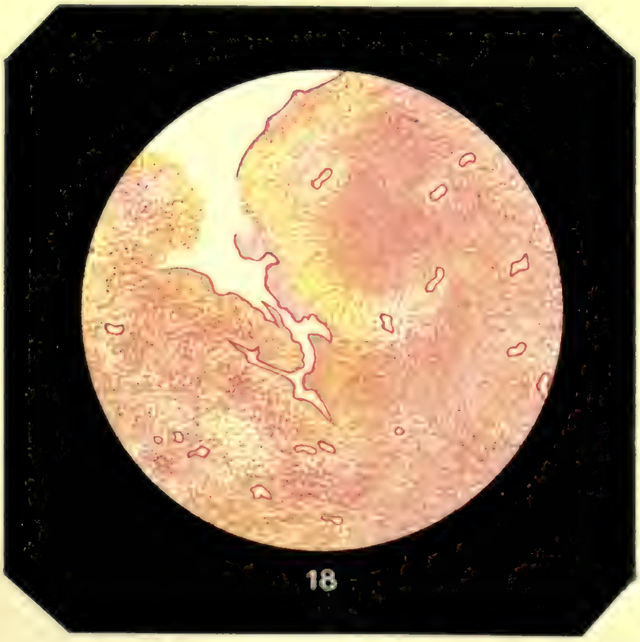

Fig. 18. Membrana dysmenorrhoica (Endometritis exfoliativa)

just mentioned; furthermore, that, in the same individual at different epochs the variations are diverse in extreme degree. Also, in cases of stenosis of the os internum in virgins as well as in other pathologic conditions, the decidua menstrualis (as I might easily prove) has been found particularly well-developed. I consider it, therefore, rather as the result of unusual stimuli than as a physiologic coadjuvant of menstruation.

Nevertheless, these changes in the mucous membranes, especially the phenomena of serrate and asteroid glands, are often in etiologic relation to menstruation. The microscopic presentment also was derived from a curetment done two days before menstruation. The patient suffered from dysmenorrhea and stenosis of the os internum. In the left half of the section is seen the longitudinal, serrate cut of a gland, while the right half contains the star-form of a gland in cross-section. Emphasis, however, must be laid upon the fact that similar phenomena occur having absolutely no connection with menstruation but due to other stimuli or irritants, as depicted in Fig. 4.

Fig. 18. Membrana dysmenorrhoica (Endometritis exfoliativa)
Alum-carmin × 30

In many instances the mucous membrane of the uterus during menstruation is cast off in larger pieces, having the appearance of shreds of skin. Their expulsion is effected by uterine contractions resembling those of childbirth, and accompanied usually by pains of considerable intensity, dysmenorrhoic. The cause of the phenomenon is not clear but there is, doubtless, some relationship with the unusually vigorous development of a decidua menstrualis.

In Fig. 18 is depicted a membrane of the dysmenorrhoic type, as cast off by the uterus. The connective tissue is markedly proliferate and saturated with blood; its cells (stroma cells) are small, punctate in appearance, and structurally, as if washed-out. There are also areas where these stroma cells are similar to those of deciduous origin. The glands, figuratively, have retired to the background; they are crumpled up, shriveled, and frequently remarkable because of their compressed dentate shapes. The epithelia of glands and mucosal surface are atrophic and the entire specimen has an inanimate, degenerate aspect.

Pregnancy

Plates X—XV. Figs. 19—30

Plate X

Fig. 19. Decidua uteri gravidi (third month)

Fig. 20. Decidual cells

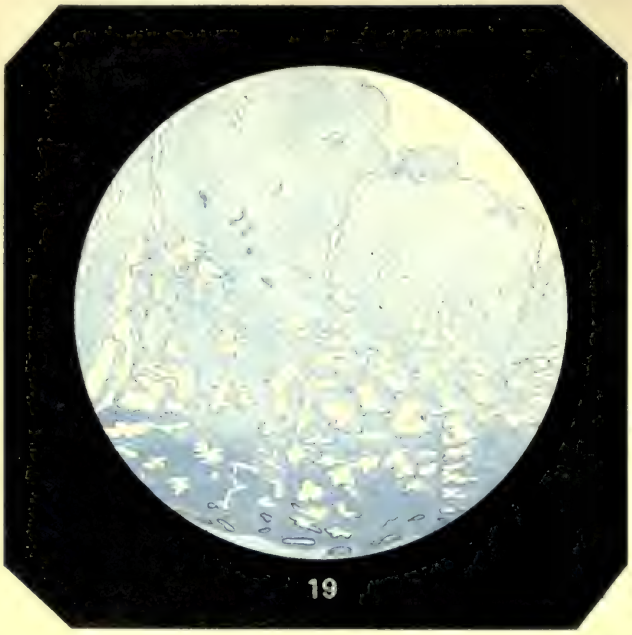
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Fig. 19. Decidua uteri gravidi (third month)

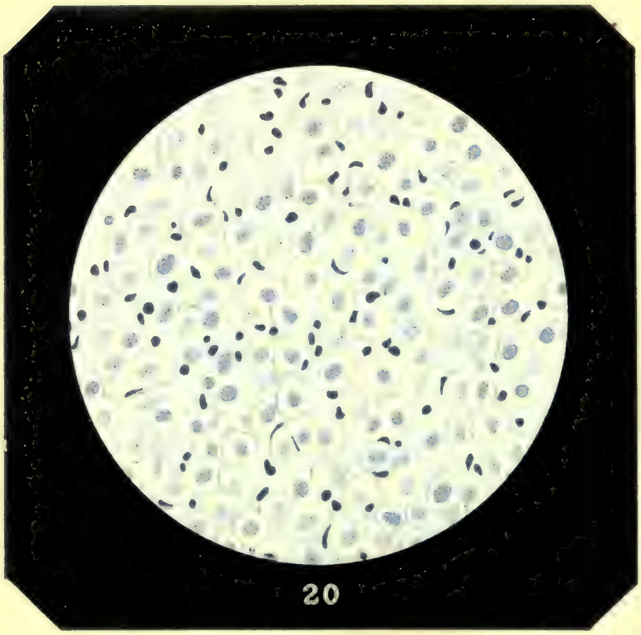
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Fig. 20. Decidual cells

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Fig. 19. Decidua uteri gravidi (third month)

Hemalum × 8

With the inception of pregnancy, the mucous membrane of the body of the uterus begins to change. Its depth (or thickness) increases appreciably and two strata may be differentiated clearly: one superior, superficial; one inferior, deep.

The upper, or pars compacta, is composed chiefly of cellular elements, the excretory ducts of the glands, like slim rods, lying far apart from one another. In the lower stratum, or pars spongiosa, the dentate, dilated glands are in vast majority.

The uterine mucosa, thus topsy-turvy, is termed: decidua graviditatis. During the later course of pregnancy, the sharp deliminations, *viz.* of glands, fade. For the microscopical diagnosis, however, the earlier months of pregnancy are more suited, particularly in the demonstration of abortion by material obtained from either curetment, or masses, expelled by uterine forces. In the section given of a decidua at three months, the substantia compacta is clearly distinct from the substantia spongiosa. Below and near the musculature, are still a few unaltered glands.

Fig. 20. Decidual cells

Hemalum × 350

The great characteristic of the decidua is the change which takes place in the stroma or connective tissue cells of the greater portion of the mucosa, but chiefly in those of the substantia compacta. Whilst stroma cells in ordinary circumstance are completely filled by their nuclei, the cells during pregnancy exhibit enormous increase of the cell-body. The cell acquires a dull, glassy appearance; its outline or contour is faint, delicate; its nucleus takes the stain better, and hence is more prominent. The cells lie in close proximity and often the contour of the cell-body becomes visible only by careful manipulation of the instrument. Between the decidual cells are, as shown in the view, some smaller cells here and there.

Decidual cells are present throughout the pregnancy and, when discovered in curetted material, are of great import in the matter of diagnosis. It is true that cells resembling those of the decidua of pregnancy may be found when the individual is not gravid, but these commonly lack the size, the blister-like form and the pale, translucent appearance.

Sarcoma cells (cf. Fig. 40) are differentiated from those of the decidua by their irregularity of outline and of nucleus. The flat epithelia of the portio (cf. Fig. 2), sometimes scraped off by the curet and somewhat resembling decidual cells, have a smaller and more punctiform nucleus, a terrace-like flattening from below upwards, and no interlying tissue.

Plate XI

Fig. 21. The glands, during pregnancy

Fig. 22. A gland, during pregnancy

Fig. 21. The glands, during pregnancy

Alum-carmin × 60

The substantia spongiosa of the decidua owes its remarkable appearance to the metamorphosis in glands. Like meshes of a net, the orifices of glands lie neighborly. These glands are very similar to the glands in endometritis glandularis hypertrophica and in decidua menstrualis. In transverse section, they are star-shaped; in longitudinal section, serrated. In general, the great dilatation and the invasion of lumina by cord-like masses may be considered quite extraordinary phenomena.

The specimen, furthermore shows that, in the substantia spongiosa of the decidua graviditatis, a transformation of connective tissue cells into decidual cells is not a "constant quality."

Fig. 22. A gland, during pregnancy

Alum-carmin × 350

With the higher power applied to a gland during pregnancy, it is plain how the glandular epithelia in several places have shoved forward and stratified, and how the cord-like prominences came into existence. The stroma or connective tissue cells directly environing the gland have, apparently because of the pressure exerted by the greatly dilated glands, been extended longitudinally and arranged in circles.

Differentiation of the glands during pregnancy from similar but malignant glandular changes is rendered possible by the fact that the epithelia during normal pregnancy are like in form and pallid in hue. Furthermore, we are considering here those cells only which here and there protrude, cord-like, into the lumen whilst in incipient, malignant stratification the proliferation of cells is much more diffuse (cf. Fig. 41).

Glands, during the pregnant state, lose later their characteristic form, and are found, finally, only as cuneiform defects in the decidua. But, even during the first period of pregnancy they are not always of so typical a morphology. Yet, in curetment undertaken to verify the diagnosis of abortion, they afford essential help, though the mere presence of glands having such morphologic qualities but unaccompanied by decidual cells or chorionic tufts does not render possible the diagnosis of abortion.

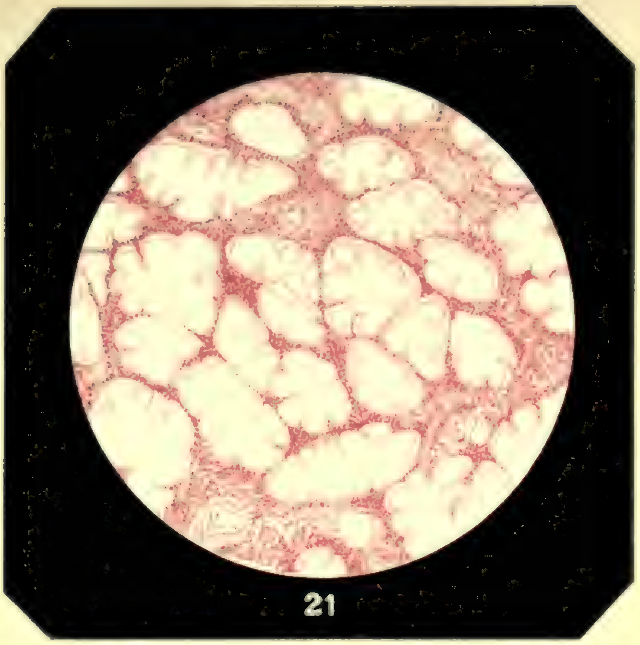

Fig. 21. Glands, during pregnancy

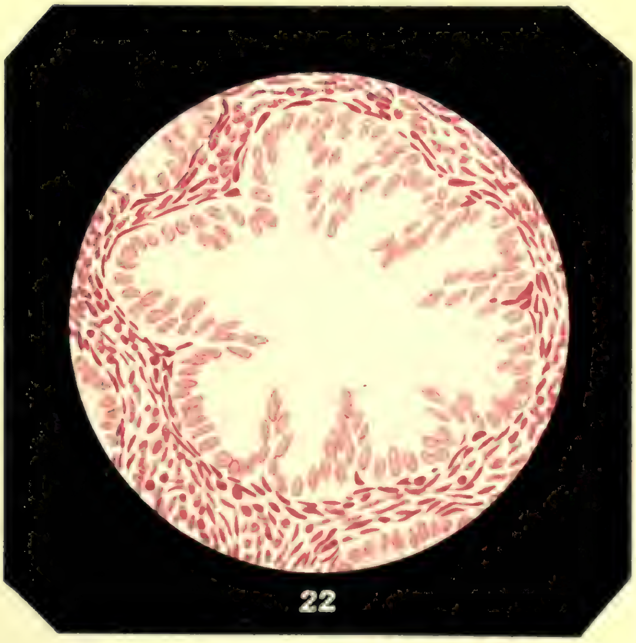

Fig. 22. A gland, during pregnancy

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Plate XII

Fig. 23. Chorionic villi, with decidua

Fig. 24. Chorionic tufts

Fig. 23. Chorionic villi, with decidua

Hemalum × 60

Of the three membranes enclosing the embryon, the outermost or decidua alone is maternal in origin. The chorion or middle and the amnion or innermost membranes are of embryonal genesis. The chorion, by its villi or tufts penetrating the decidua, provides for the nourishment of the unborn. During the first period of pregnancy, the entire outer surface of the chorion is covered with villi, but later these, for the most part, regress and disappear until, finally, they are found only within a certain area, commonly around the place of attachment of the ovum. Here their growth is enormous and leads to the development of the placenta. The nourishment of the embryon, primarily osmotic only, is accomplished, by an exchange of bloods, maternal and fetal. Within the villi of the chorion blood-vessels are formed and these vascularized chorionic tufts penetrating the decidua sway in the pulsing currents and passioned vortices of maternal blood.

Where the chorionic villi come in touch with the decidua, there develops a more or less firm intergrowth, bridges made of cells forming between. In the figure they are to be seen in the center and the right side, while the other villi (from the upper part of the section, down) float free in the intervillous area. The lower half of the specimen includes the decidua, some of its glands and a small portion of muscle tissue.

Fig. 24. Chorionic villi

Hemalum × 350

Chorionic villi are composed of connective tissue stroma and a surface made up of two layers or strata of epithelia. The stroma contains connective tissue cells rather elongated in shape and scanty in number, and serves as support to the blood-vessels when these are formed. The double covering or surface of ectodermal epithelia, the "chorionic epithelia," is formed of an inner stratum of large polygonal cells with small round nuclei, the so-called "*Langhans*' cells," and an outer stratum of cells, the "syncytium."

While *Langhans*' cells are distinct in contour, the outer layer of epithelia is composed of interlacing strings of cells unbroken in continuity. Their outlines have entirely disappeared and only the nuclei are discernible. This conglomeration of cell elements, because of its remarkable structural composition, is termed: syncytium; it stains well.

Langhans' cells and the syncytium form then, together, the chorionic epithelium, which, even under normal conditions, may exhibit an abnormal proliferation. The syncytium develops cuneiform, or, club-like sproutings; some cells here and there break away and may be found even in the superficial strata of uterine muscles: syncytial errant cells. *Langhans*' cell stratum is broken through by the syncytium which crowds onward to the decidua and thus are formed the anchoring villi, depicted in Fig. 23 and discussed in the text thereof.

The villi of the chorion change in appearance during the months of pregnancy. While at first *Langhans*' cells and the syncytium are distinctly cognizable as such (shown in the section), in the later months and in the mature placenta the syncytium alone is visible. The club-like growths are no longer found, but the blood-channels, on the contrary, are plainly seen in the interior of the villi though, at the time when the specimen was obtained, these had not yet evolved.

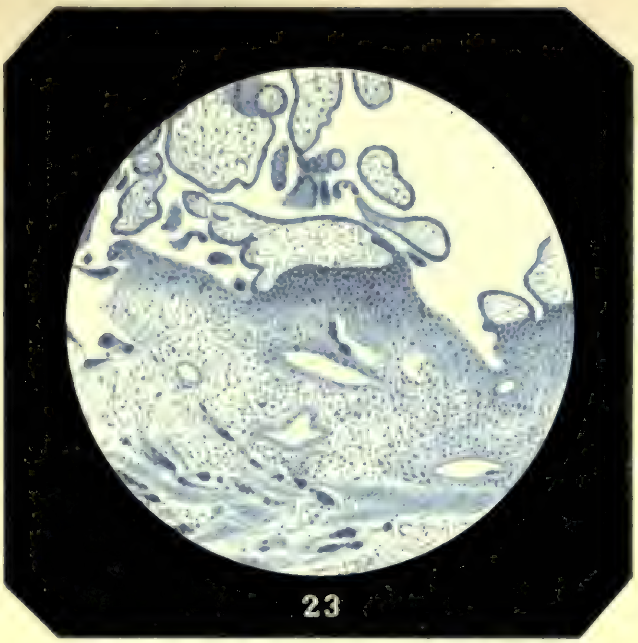

Fig. 23. Chorionic villi and decidua

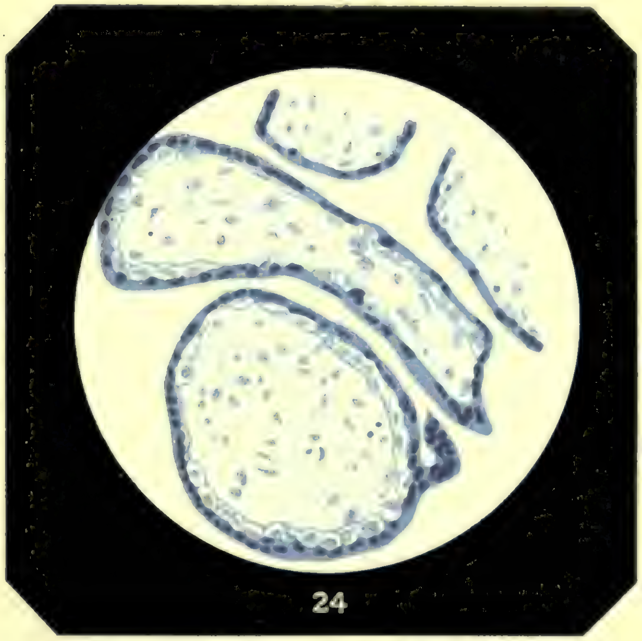

Fig. 24. Villi of the chorion

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Plate XIII

Figs. 25–26. Retention after abortion

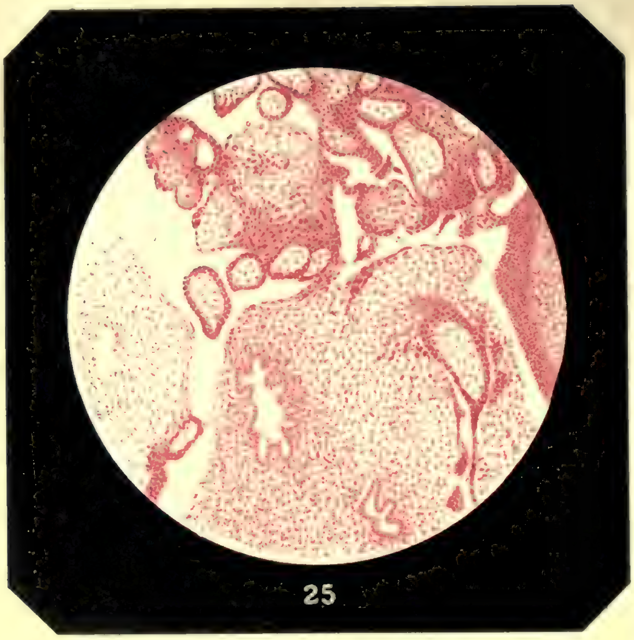

Fig. 25. Retentio post abortum

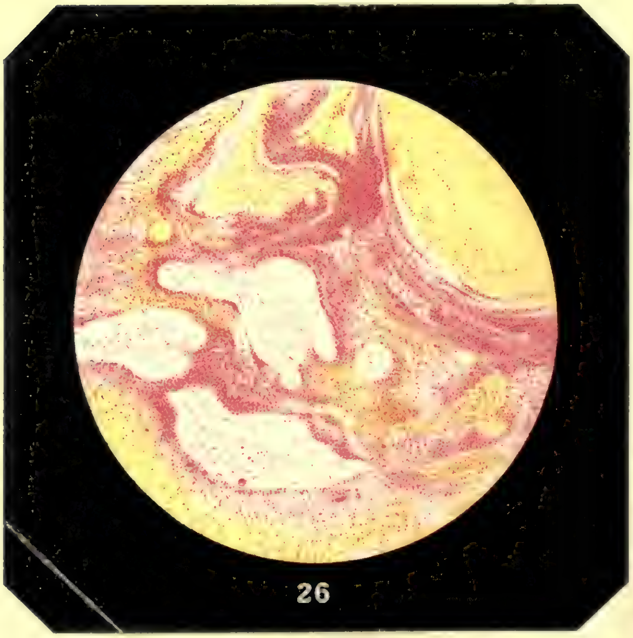

Fig. 26. Retentio post abortum

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Fig. 25. Retention after abortion

Alum-carmin × 60

Irregular bleedings in women not past the child-bearing age are often due to the residua of an abortion. It is not always possible to establish, clinically, the diagnosis of abortus incompletus, and the curetment, undertaken for therapeutic purpose, should be followed by microscopic examination of curetted material in order to exclude other causes of irregular hemorrhages, *e. g.*, malignant disease.

The diagnosis of retentio post abortum may then be positively established when chorionic villi, *i. e.*, embryonal residua, are present in the specimen. Decidual cells and the altered glands common to pregnancy may also alone verify the diagnosis of status post abortum if they be characteristically developed, yet it must be borne in mind that the connective tissue cells of mucous membrane may, on occasion, undergo a morphologic change into forms similar to decidual cells though no pregnancy exist, and that certain gland formations in endometritis glandularis and in the menstrual decidua may much resemble gland forms in pregnancy.

The specimen of curetted material here presented shows decidual cells, the glands of pregnancy and chorionic villi; we are, therefore, dealing with products due to a state of pregnancy. Were the chorionic villi lacking, the diagnosis of status post abortum would, it is true, be probable but not absolutely certain.

The chorionic villi are seen in the upper half of the section irregularly dispersed and varying in size. They permit recognition of the darker contour of chorionic epithelia and the lighter central portion of connective tissue. At various points cell proliferation of the chorionic epithelium is discernible. In the piece of decidua occupying the lower half of the preparation are seen two star-shaped glands of the pregnant state.

Fig. 26. Retention, after abortion

Alum-carmin × 60

Not only does further continuance of the state of pregnancy develop certain changes in chorionic villi, but continued retention within the uterus is also capable of such development. Such metamorphosis, then, is to be considered as a gradual disintegration of the villi. These lose their finer structure, appear washed-out, and the chorionic epithelium is no longer demonstrable. Nevertheless, from such pictures, misty with degeneration and decay, it is often possible to diagnose what was a villus of the chorion and, therewith, the former pregnant state. In such case the villi are seen as rather long, streaky, most commonly bent or curved portions of tissue, lying in a field composed, for the most part, of blood and fibrin. Sometimes, decidual cells, glands of pregnancy or villi in a better state of preservation are discernible.

In the view here presented, the four clear areas are washed-out villi, showing very little, however, of their former regular contour and with traces only of chorionic epithelium. But, their sharp delimitation against the circumjacent mass with its streakedness of texture, the quantity of blood, fibrin, round-cell agglomeration afford a picture the genesis of which is possible only to curettage following abortion.

Plate XIV

Figs. 27 and 28. Hydatiform mole (German: Blasenmole). Myxoma chorii

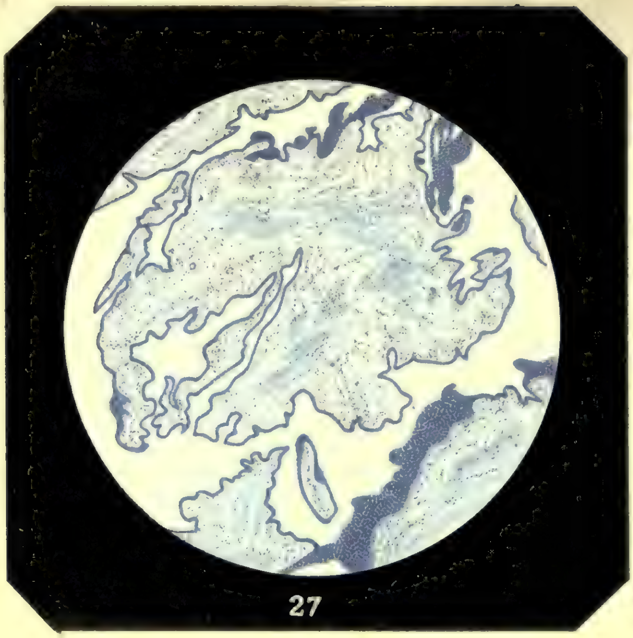

Fig. 27. Hydatiform mole. Myxoma chorii

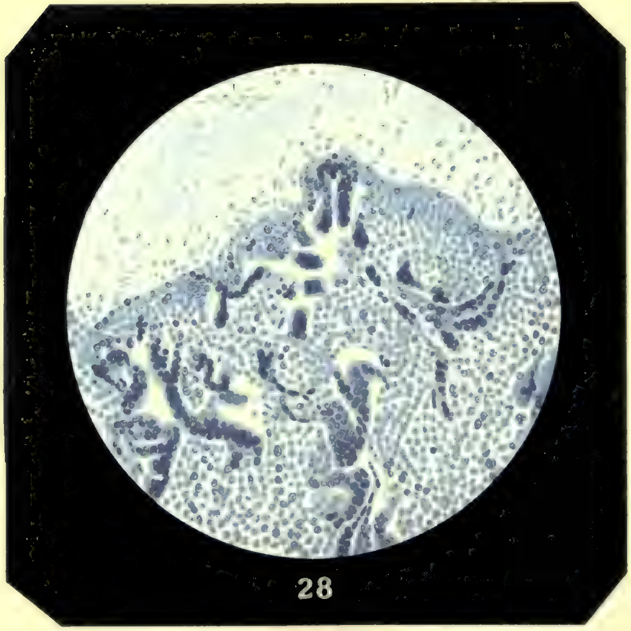

Fig. 28. Hydatiform mole. Myxoma chorii

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Fig. 27. Hydatiform mole. Myxoma chorii

Hemalum × 12

When the chorionic tufts are transformed into bleb-like structures much resembling bunches of small white grapes, we have what is called the hydatiform (hydatos: water) mole or myxoma chorii. The villi become distended with fluid and the vesicles or watery cysts hang like clusters of grapes. This metamorphosis may evolve at any time during gravidity, including the whole chorion or placenta or the process may be limited to greater or less areas. When fully developed, the somewhat movable vesicles, held together in a loose-textured supporting tissue, are at once recognized as forming a hydatiform mole. Sometimes, however, its diagnosis is required on examination of material afforded by a curetment or passed involuntarily.

Microscopically, a chorionic villus thus altered may not have the typical cystic hollow at its center but the change is, nevertheless, unmistakable. The connective tissue cells of the villus lose their nuclei save, possibly, in cells superficially placed, and there remains a structureless mass of degenerate tissue. The chorionic epithelia also undergo vital metamorphosis, chiefly proliferative in character. When half through its degenerative transformation, the villus is enlarged, of irregular form, internally broken-down and its epithelium noticeably proliferant. In the right upper region of the figure the slender pedicle is to be seen.

Fig. 28. Hydatiform mole. Myxoma chorii

Hemalum × 140

With increased magnification we observe, chiefly, the pronounced and erratic proliferation of chorionic epithelium. The syncytium shows odd protuberation, eccentric bulgings, sometimes vacuoles also. Groups of cells push out and, as syncytial wanderers, sink deep into adjacent tissue. *Langhans*' cell-stratum takes on Brobdingnagian dimension and may roll, proliferant, over the syncytial surface and build micro-mountains of cells.

The upper third of the figure is occupied by degenerated stroma.

Plate XV

Figs. 29–30. Syncytioma or Chorioepithelioma malignum

Fig. 29. Syncytioma or Chorioepithelioma malignum

Hemalum *Van Gieson's* Stain × 84

Syncytioma malignum is an extremely malignant neoplasm, born within the womb. It develops only during the child-bearing years of the patient's life and only during a pregnancy; apparently, with especial frequence as sequela to hydatiform mole.

Under the microscope it is seen to be composed of the two cell forms of chorionic epithelium, the syncytic and *Langhans'* cells. Irregular conglomerations of cells form, the components of which are partly proliferate syncytium, partly *Langhans'* epithelium. In the section, the syncytial groups are shown as diffuse brownish masses, of which the large nuclei alone stand out distinct. *Langhans'* cells invariably have cell contour and often resemble cells of the decidua. In chorioepithelioma malignum they are in irregular groups (stained blue in the figure) and, under higher power, exhibit nuclear division.

The differential diagnosis, with regard to the benign myxoma chorii, which also displays proliferation of chorionic epithelia, is established by another factor, microscopically present, *viz.*, the invariably distinct destructive action upon surrounding tissue. In the view, for example, the musculature to the right is appreciable only as a streaky mass, difficultly stained, and, furthermore, diffuse hemorrhages are present.

The two varieties of epithelium are not always present in a section; sometimes a number of sections have to be cut. The tumor itself contains no vascular channels but it often breaks through the walls of those belonging to its matrix tissues, the chiefest characteristic of this neoplasm being its limitless power of growth.

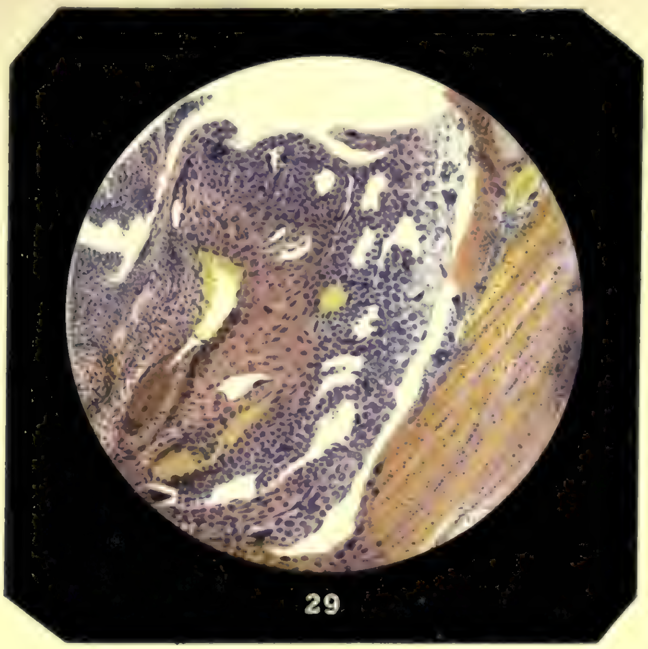

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Fig. 29. Syncytioma, or Chorioepithelioma malignum

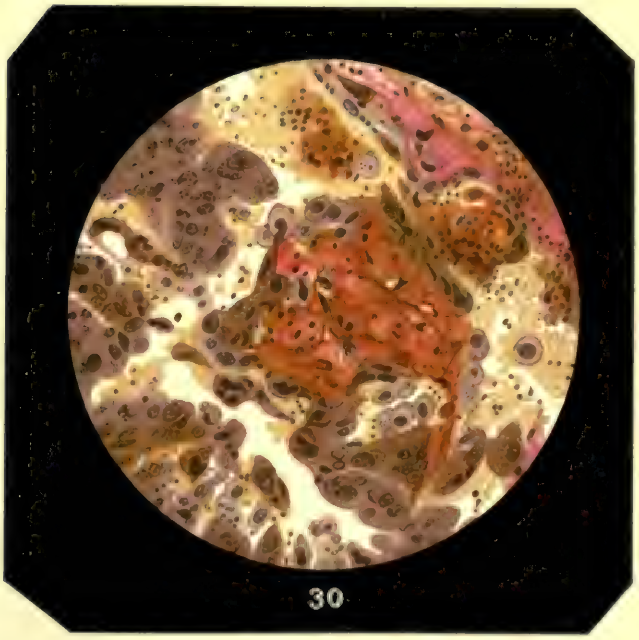

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Fig. 30. Syncytioma, or Chorioepithelioma malignum

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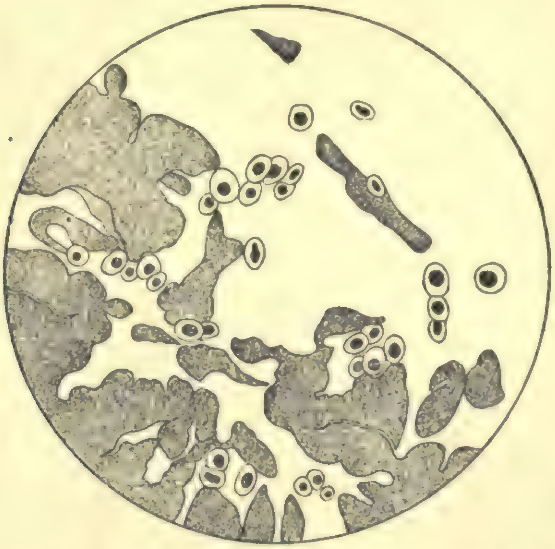
Fig. 30. Syncytioma or Chorioepithelioma malignum

Hemalum *Van Gieson* × 450

Another peculiarity of chorioepithelioma is its ability in metastasis. Its metastatic operations are carried on by way of the blood channels and may attain to organs most diverse: lung, liver, encephalon, etc., and not infrequently it is the cause of death. The metastatic colonization is always identic in its microscopic essentials with the mother-neoplasm, and, in the organs affected we find the proliferate masses of syncytial and *Langhans'* cells.



The individual cells are those of Langhans. The dark areas are syncytial masses. Their nuclei are not depicted here; true, also, of erythrocytes and necrotic tissue,—for the sake of generalization.

Then compact nodes form, soon tumescent, dilating, extending. In the immediate vicinity of the metastasis there is often naught left of the original histologic constitution of the organ implicated, for, the destructive action of the neoplastic tissue is as potent here as it was within the uterus. In the neighborhood of tumor-cells lie stricken, death-done, structureless and blood-drenched masses alone.

The view presented comes from a pulmonic metastasis, the structure of the organ being no longer cognizable. With increased magnification, the differences betwixt the diffuse, dark syncytial masses and the compact and brighter *Langhans'* cells are made particularly distinct.

Carcinoma uteri

Plates XVI—XXI Figs. 31—42

Plate XVI

Figs. 31 and 32. Carcinoma portionis

Fig. 31. Carcinoma portionis

Alum-carmin × 112

Carcinoma, wherever evolved, is an epithelial new-growth and its essential elements, whether flat or cylindric, proliferate unceasing and limitlessly into environing tissues. Whence are developed the various forms, classified by reason of their manner of growth and by the quality of their epithelium.

As the portio vaginalis uteri is, normally, surfaced with flat epithelium, the ordinary carcinoma portionis is of this epithelial variety. From its superficies masses and cords of epithelia sink into the adjacent original tissue, shove it aside and destroy it. In this tissue, hollows or cavities are formed, filled with proliferant epithelia and dubbed: cancer alveoli. These carcinomatous alveoli may be, comparatively, quite large and of round or oval form, or, they may extend in long, slim wedges or cords, corresponding to lymph-spaces. But ever vitai, essential is the monstrous proliferation and the epithelial advance into other tissues. Cancerous tissue has no vascular channels but is nourished by its circumjacent hosts.

The view shows cancer-alveoli as darker cell-complexes, lying within the surrounding brighter tissue of the portio vaginalis. The alveoli are composed of masses of flat epithelia derived, primarily, from the flat epithelium covering the portio. This "derivative" relationship, however, concerns only the surface of the portio and, because of the rapid destruction of the latter, is demonstrable only at the beginning of the disease. A small piece of a suspected portio, excised or scraped off, and subjected to microscopic investigation, will, ordinarily, show no connection with the original superficies, as in our own case (Fig. 31).

Cylindric-cell carcinoma also may appear on the portio vaginalis uteri, developing upon eroded areas as matrix tissues when cylindric epithelia have found lodgment on the portio. These forms are less frequent but identical, otherwise, with the cylindric-cell carcinomata found in the uterus:

Fig. 32. Carcinoma portionis

Alum-carmin × 750

In general, the study of cancer specimens under the lower powers is to be recommended, for, with the wider vision the contrasts between masses of epithelia and the normal tissue become plainer. In many instances, nevertheless, it may be necessary to use higher powers, namely, when the specimen is composed of cancerous tissue alone, all else having been annihilated.

The "cancer cells" or the epithelia found in abnormal proliferation, show certain variations from healthy epithelial cells. Thus, cancer cells are irregular in the form and size of cell and nucleus; there appear giant-cells and frequent, atypic karyokinetic changes. Whilst normal epithelia exhibit simple, regular structure, cancer cells are always astoundingly unlike among themselves; in the section, scarcely one cell resembles any other.

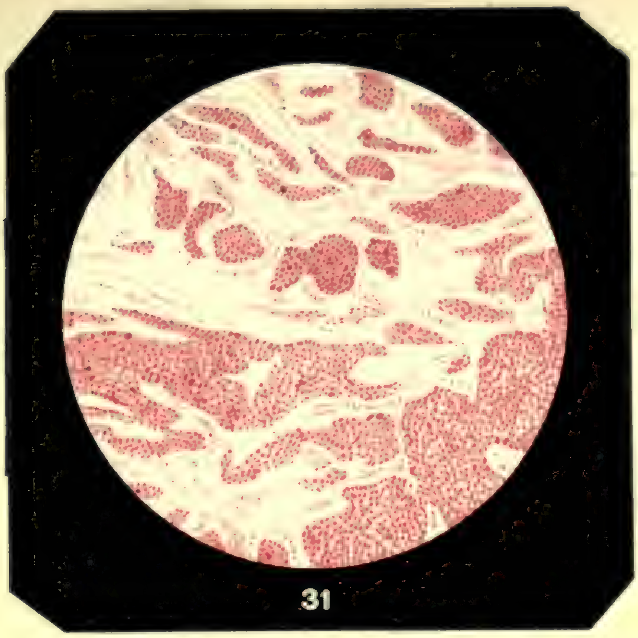


Fig. 31. Carcinoma portionis

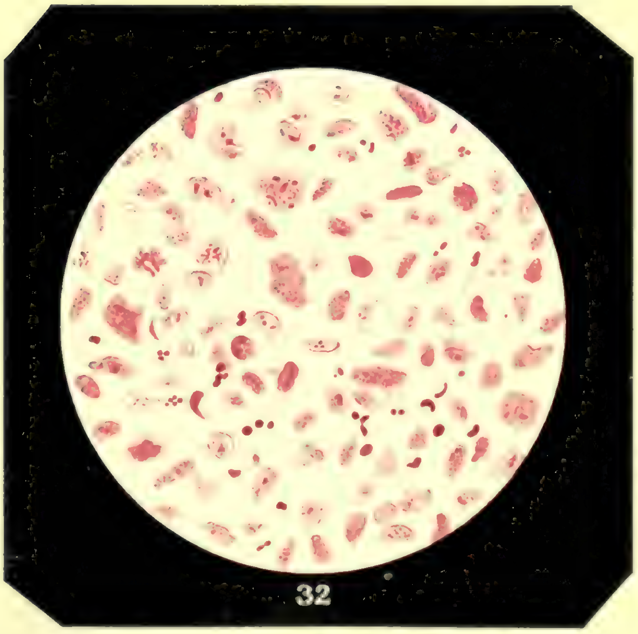


Fig. 32. Carcinoma portionis

Plate XVII

Fig. 33. Carcinoma cervicis. Flat epithelium cancer

Fig. 34. Carcinoma cervicis. Cylindric epithelium cancer

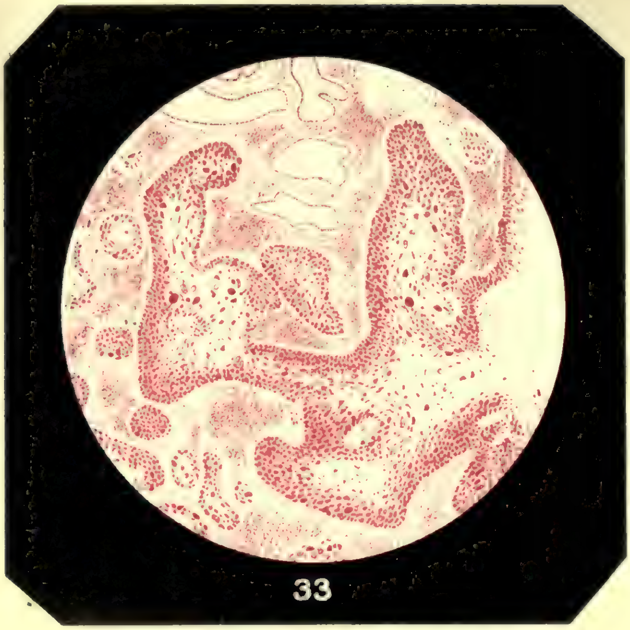


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Fig. 33. Carcinoma cervicis. Flat epithelium cancer

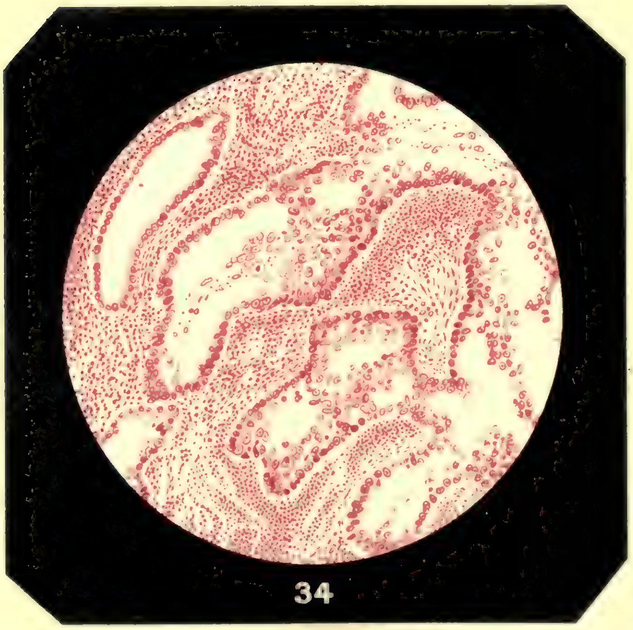

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Fig. 34. Carcinoma cervicis. Cylindric epithelium cancer

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Fig. 33. Carcinoma cervicis. Flat epithelium cancer

Alum-carmin × 84

Though the cervix has a surface of cylindric epithelium, carcinomata of flat epithelium are also found. From its superficies, broad masses of flat epithelial cells grow burrowing into the depths. They encircle glands almost perfect of structure or else drive through them until, finally, all tissue is filled with cancer alveoli.

In but one preparation of a flat epithelium cancer there is frequently naught found indicative of its origin; contrarily, it may hap that glands with cervix epithelia are still present. This, in our case, is the fact, observable in the upper part of the figure. From the right, an enormous, ramifying mass of carcinomatous tissue drives toward the center while smaller areas of flat epithelium are seen in the left and lower margins of the section.

Fig. 34. Carcinoma cervicis. Cylindric epithelium cancer

Alum-carmin × 112

Cylindric epithelium carcinoma of the cervix is commoner, taking origin in the epithelia of the cervical surface and in the glands, where cylindrics proliferate and foregather in strata, cell upon cell, until glands are filled entirely. Simultaneously, the depths are further stirred by invasive masses of epithelia, dominating greater areas and breaking into the musculature. Then the cylindric cells soon lose their typical form, pressed together and, at last, made polygonal by their own massing.

In the large and already confluent glands of the specimen, the epithelial cells are found in obvious stratification, as though the entire lumen had been filled by degrees. In the upper left corner of the section is a gland still approximately normal in appearance.

Plate XVIII

Fig. 35. Carcinoma corporis. Flat epithelium cancer

Fig. 36. Carcinoma corporis. Adenocarcinoma

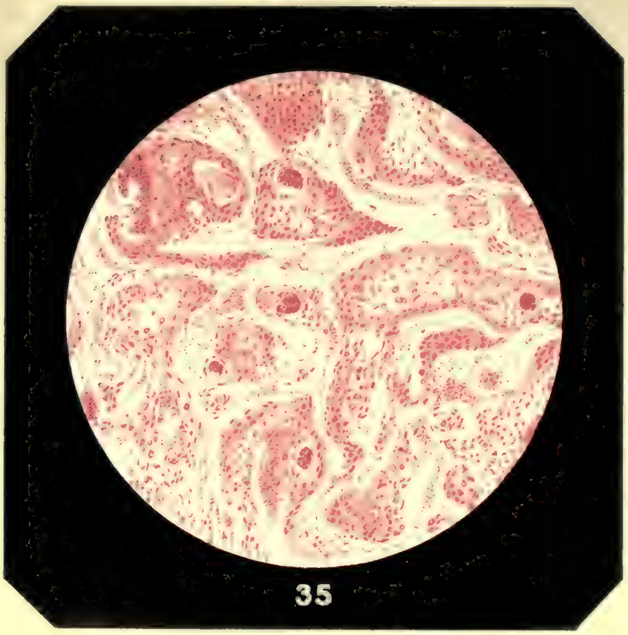

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Fig. 35. Carcinoma corporis. Flat epithelium cancer

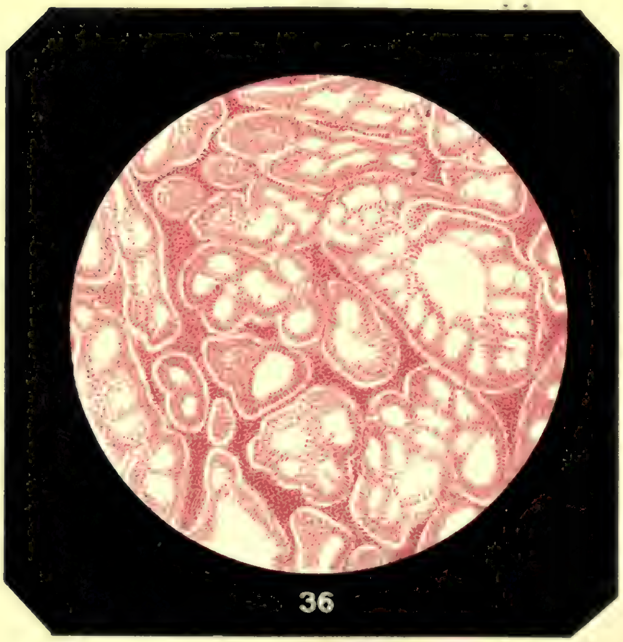

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Fig. 36. Carcinoma corporis. Adenocarcinoma

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Fig. 35. Carcinoma corporis. Flat epithelium cancer

Alum-carmin × 112

In the corpus uteri also, cancer of either the flat or the cylindric epithelium variety occurs. The flat epithelium growth has the same microscopic appearance here as in cervix or portio vaginalis: islets of epithelia in the tissues of the corpus, filling cancer alveoli of various form and magnitude. In the center of the epithelial mass are not infrequently found degenerative changes, a common and characteristic phenomenon in all flat epithelium cancers. Together with softening and disintegration, the cancer "pearls," like those in cancroids or squamous epitheliomata, are occasionally observed.

In the view, very little normal tissue is present, while cancer nests and plugs lie about everywhere. In the interior of some alveoli structural changes of cell to the round or polygonal form indicate degenerative processes in operation.

Fig. 36. Carcinoma corporis. Adenocarcinoma

Alum-carmin × 84

Correspondent with the cylindric epithelium normally present in the corpus uteri, the common carcinoma corporis is also cylindric epithelium cancer. Unceasingly, the glands are filled with epithelial proliferations until there is no more available space. Then it may be difficult to distinguish these glands, filled to bursting with epithelial cells, from the alveoli of a flat epithelium cancer. Interstices still present in the epithelial mass may appear in the microscopic field as perforations or windows. In other areas it may be possible to apprehend the process of stratification in its incipiency, and thus determine the origin of the cancer as cylindric epithelium.

The carcinomatous glands in the section are seen distinct against the meager interstitial tissue still present. They are notably increased in size and filled with masses of epithelial, showing numerous apertures in both central and marginal zones.

Plate XIX

Fig. 37. Adenoma malignum corporis uteri evertens incipiens

Fig. 38. Adenoma malignum corporis uteri evertens

Fig. 37. Adenoma malignum corporis uteri evertens incipiens

Alum-carmin × 30

Among the uterine carcinomata, the adenoma malignum takes unique rank. In other cancers, proliferation and stratification of epithelia are recognized, but with adenoma malignum excessive growth of the glands themselves is characteristic of its neoplastic moulding of epithelial tissue. Concomitantly, the walls of neighboring glands show distensions, bulgings, or, with the gland imminently ahead, indentation, cavings-in, collapse of its lumen.

Therewith two different forms are classified, to wit: adenoma malignum evertens, and, adenoma malignum invertens. Nevertheless, it is not always possible to differentiate, for these local increases and decreases in the lumen are more or less related, may even interchange, or, may appear together in the same specimen. The essential, vital characteristic of adenoma malignum, however, will always be its limitless potency of glandular proliferation and ramification. No longer are we dealing with a genesis of simple or tortuous glands for the microscopic field is compact with numerous and ever-branching cords, wedges, plugs and masses of epithelial cells

The section shows the more rarely observed form of incipient adenoma malignum, the finger-like processes of its glands extending into the tissues. The individual glands are still determinable, but already the dominant concept is that of errant and limitless growth.

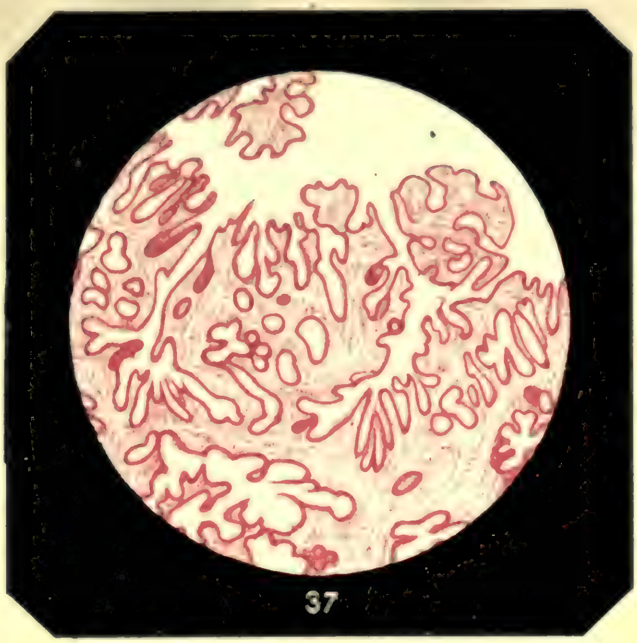

Fig. 37. Adenoma malignum corporis uteri evertens incipiens

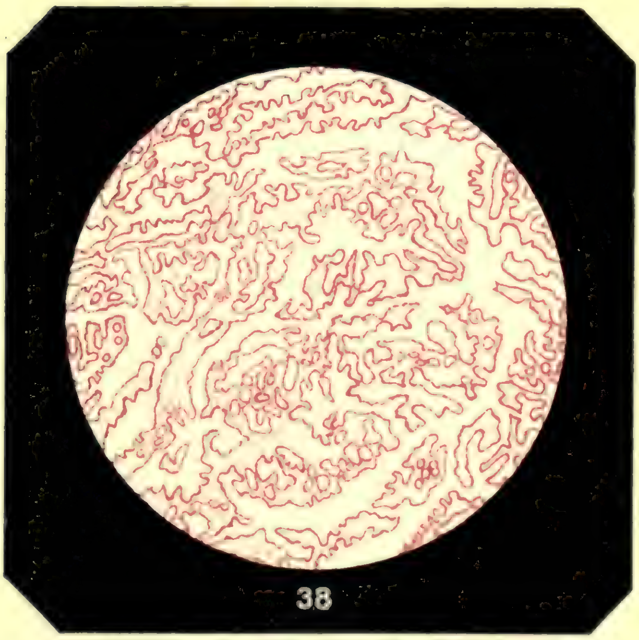

Fig. 38. Adenoma malignum corporis uteri evertens

Fig. 38. Adenoma malignum corporis uteri evertens

Alum-carmin × 12

Adenoma malignum may develop in any part of the mucous membrane of the uterus, but is, by far, most common to the corpus, rarer in the cervix, and least often found in the portio vaginalis. The neoplastic glands, unlike the morbid processes of many other forms of cancer, do not increase superficially and over large areas but plunge into the depths.

This manner of glandular polychotomy is to be considered malignant and requiring no further investigation, only when found in the uterus; in other parts of the human economy similar developments may occur quite entitled to contemplation as absolutely benign. Hence, in so far as the uterus is concerned, it is not a matter of comparison with these extra-genital growths but of differentiating from the benign uterine gland this malignant entity with its limitless capacity for proliferation and ramification.

In the section presented, a mucosal proliferation of the sort is to be sharply differentiated from a benign process having its seat in the mucous membrane of the same organ. In the most violent endometritis of the glandular type, the individual gland is still always apparent as an entity, as an individual, whilst here, contrarily, there is naught to be seen save uninterrupted, lawless epithelial processes.

As an illustration of the everting or locally distended type, the section is notable because of the distinct lateral bulgings shown in the glandular walls. Moreover, as an item of differential diagnosis, the depth of a microtomic cut separates the arboreal branchings from their trunk and hangs them isolate in the view, while adenoma of the inverting type, because of growth into the lumen, longer preserves the impression of structural unity.

Plate XX

Fig. 39. Adenoma malignum corporis uteri evertens

Fig. 40. Adenoma malignum corporis uteri invertens

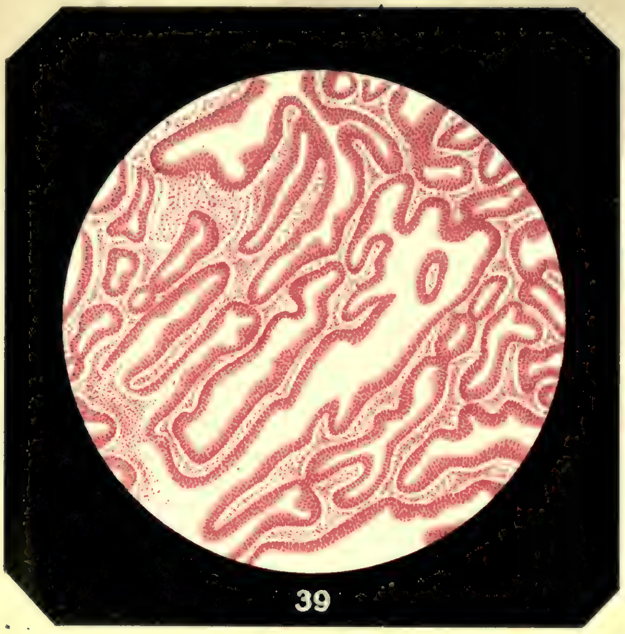

Fig. 39. Adenoma malignum corporis uteri evertens

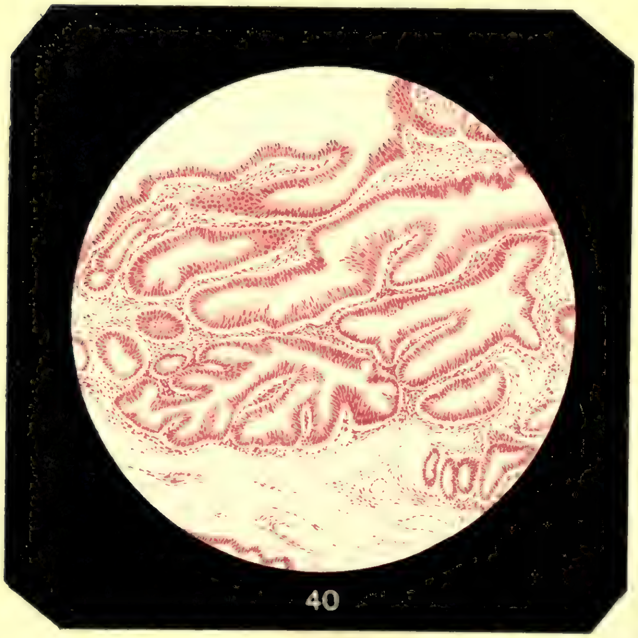

Fig. 40. Adenoma malignum corporis uteri invertens

Fig. 39. Adenoma malignum corporis uteri evertens

Alum-carmin × 60 .

By greater magnification, the difference between normal glands and the epithelial pipes of adenoma malignum is more distinctly seen. The latter are strown endlessly over the field and, furthermore, certain hall-marks are stamped upon their epithelia. The form and location of the nuclei are patterns of irregularity and karyokinesis is common.

The malignancy of the neoplasm is peculiarly easy of recognition when simultaneous stratification of epithelia is present, though this is, by no means, an essentially necessary by-phenomenon of adenoma malignum; if lacking, the evil character of the growth must, nevertheless, have diagnosis. In the figure, the everting form is again presented, for the thick, irregular branchings soon abandon the parent stem, and greater or lesser gland-complexes, apparently without any direct connection, lie side by side.

Fig. 40. Adenoma malignum corporis uteri invertens

Alum-carmin × 84

An important differential characteristic of adenoma malignum is the close contiguity of its epithelial tubes. These may lie in such intimate proximity that there is barely space for connective tissue, often but a single row of flattened stroma cells between, and not rarely the epithelia are observed base to base (cf. Fig. 39).

This characteristic, essential in diagnosing the malignancy of these glands, is present in adenoma malignum invertens in the isolate or individual glandular channels, for the invagination of their walls shoves together the bases of the epithelial cells. In the inverting form also, stratification is much more common, and, upon the invaginated parietes new epithelial cells sprout into the lumen of the gland.

The larger glands in the section are provided with many inversions of the sort, each backed by but a narrow line of interstitial tissue, or none, in which case the epithelia furnish their own backing, reciprocally. Differentially, stratification is also present.

Positive knowledge as to the presence of the inverting or the everting form in an adenoma malignum is not essential and is often impossible, but, the recognition of all these forms as malignant is absolutely indispensable.

Plate XXI

Fig. 41. Adenocarcinoma corporis uteri incipiens

Fig. 42. Deception: a Study

Fig. 41. Adenocarcinoma corporis uteri incipiens

Alum-carmin × 112

The essential characteristic of glandular cancer is epithelial stratification. The morphology of the gland itself may remain almost undisturbed. For example, in the beginning of the morbidity the centripetal buddings of the epithelial cells alone are present.

But, it is not every stratified phenomenon observed that spells: carcinoma, for epithelial stratification is occasionally noted in the glands of pregnancy, menstruation and in some varieties of endometritis. Its malignant character is to be recognized by the irregularity of its growth and by a greater degree of stratification than is proper with benign deviations from norm. About it is a certain villainous air, indicating malignancy of character.

Incipient cases are peculiarly difficult of diagnosis for, although stratification is present, it is but little advanced, so that only one, at the most, two layers of cells rise from the basic stratum. If dubiety looms large, and the investigator is not able to give decision, it is recommended that curetment be repeated after a month or so. Comparison of the microscopic aspects of the two curetments will then render decision possible. Further, the preparation and observation of several sections from different portions of material got by a single curetment will often much facilitate the acquisition of a diagnosis.

Where the process is more advanced it is not difficult of diagnosis. The epithelia gorge the distended glands to further repletion until there remain unfilled only small spaces, centrally located, or else the glands are completely filled, presenting, with the

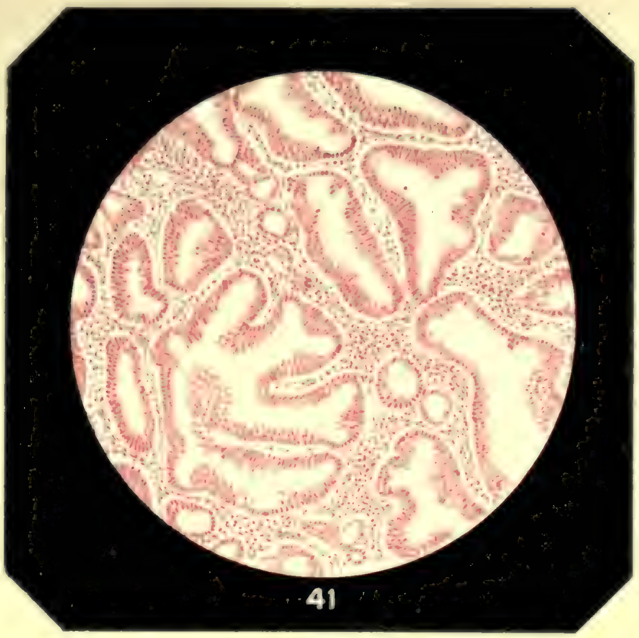

Fig. 41. Adenocarcinoma corporis uteri incipiens

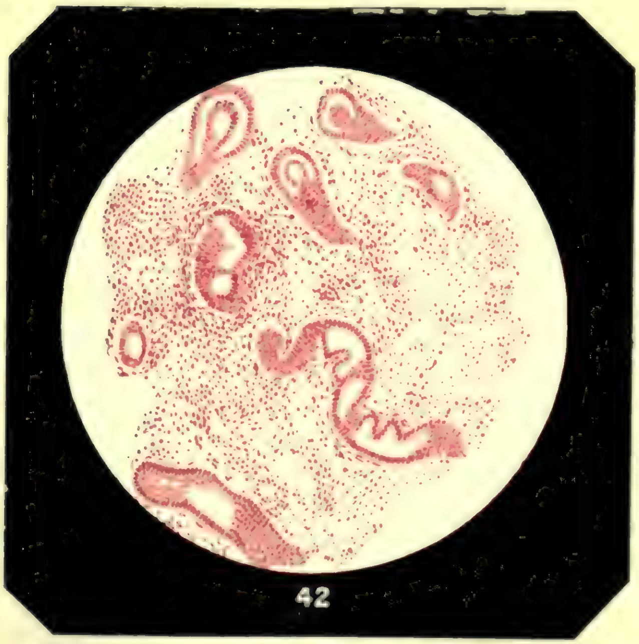

Fig. 42. Deception: a Study

further course of the affection, an appearance similar to that of the alveoli in a flat epithelium cancer. Therewith it may happen that, in other areas of the specimen studied, normal epithelium may be found or, as in our figure, an incipient stratification discovered.

The combination of adenocarcinoma with adenoma malignum (q. v.) is not rare and renders easier a diagnosis of malignancy. In which case, together with epithelial stratification, we have the illimitable proliferation of gland like tubes.

Fig. 42. Deception: a Study

Alum-carmin × 112

The recognition of stratification in the parietes of a gland requires extremely careful investigation, *i. e.*, by employing the higher-powered objectives, for there are specimens showing glands, which, superficially observed, are deceptive in the concept of stratification conveyed. In the first place, this may occur when the tip or cul-de-sac of a gland has been included in the section, so that by a transverse cut several rows of epithelia, apparently, lie in juxtaposition and parallel; secondly, because in preparing the specimen, invagination of the gland wall took place and thus, in section, more than one stratum of epithelium was seen.

Deceptive views of this sort are invariably to be differentiated from true stratification by the fact that in the latter phenomenon all the cells in parallel include and present their nuclei to the microtomic incidence. Contrarily, the transverse cut in pseudostratification passes through the nuclei of one stratum while the other rows exhibit an incidence without nuclei, the knife passing through only the apices of cells. In genuine stratification, therefore, the nuclei are evident in all the cell rows; in the pseudo-case, less and less of nucleus and cell is seen.

Where the section has been cut too thick, particular caution is needed, for, superficially observed, it is not difficult to behold several rows of cells in pleasing parallel. Zealous use of the micrometer screw, however, together with greater magnification will demonstrate in these cases that one cell stratum alone is sharply defined, the adjacent row showing a lower or higher plane of section.

Bulging inward of the gland wall, into its lumen, so-called invagination, is never indicative of malignancy. It is frequently seen in endometritis when the growing gland is not able to progress farther in the direction of its longitudinal axis. In such case, transverse section shows the lumen of one gland encircled by that of another.

In the figure, the glands are located in very loose-textured connective tissue. All of them are provided with apparent aggregations of epithelia and epithelial strata, but, actually, the condition is entirely benign. The three upper glands display also, invaginations.

Polypus cervicis

Plate XXII. Figs. 43 and 44

Plate XXII

Fig. 43. Benign polyp of the cervical mucosa

Fig. 44. Carcinomatous polyp of the cervical mucosa

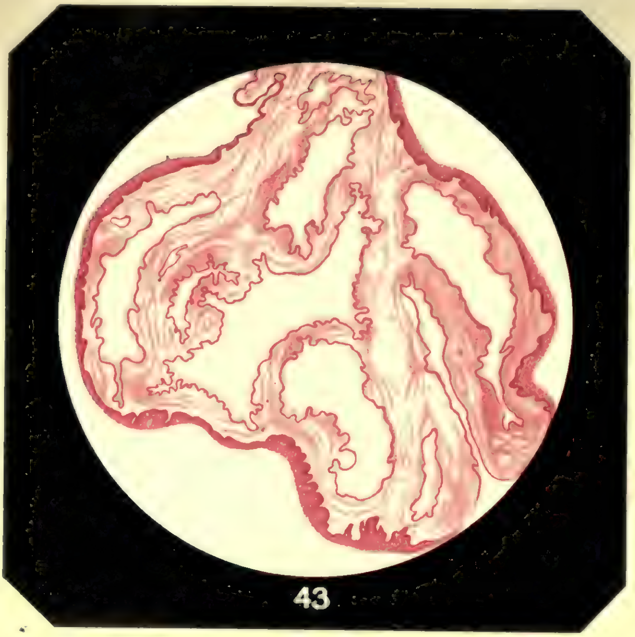

Fig. 43. Benign polyp of the cervical mucosa

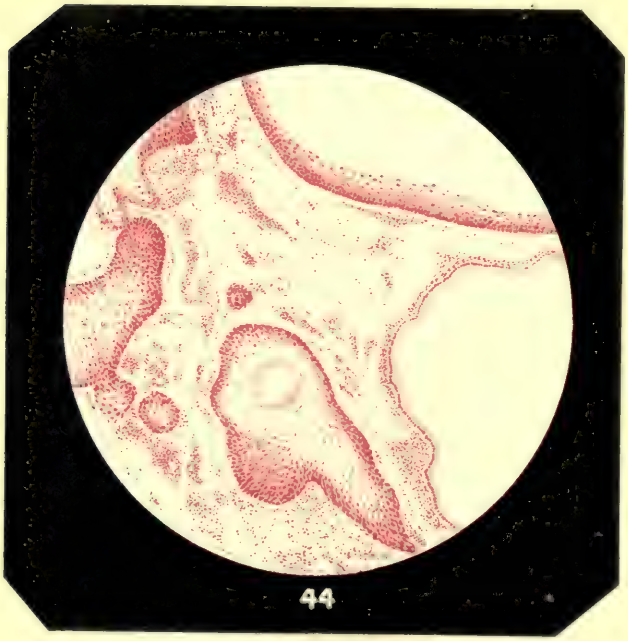

Fig. 44. Carcinomatous polyp of the cervical mucosa

Rebman Company, New York

Fig. 43. Benign polyp of the cervical mucosa

Alum-carmin × 8

Quite as circumscribed areas of the uterine mucous membrane are capable of proliferation and then of rising above the mucosal plane by means of pedicles (cf. Fig. 8), so likewise within the lumen of the cervix, polypous growths occur. These also are instrumental in the matter of hemorrhages, but are much more easily diagnosed, for their peregrinations are always confined to the cervical canal, and, pediculated, they may lie within the os externum: As nodulated growths they may be felt and seen at this point for, ordinarily, they are the size of peas, though they may exceed that of a cherry.

The microscopic examination makes plain the structure of cervical mucous membrane: branched acinous glands and high cylindric epithelia with nuclei basically located. In the section here presented, the microtome caught, inclusively, the slim stem of the polyp. The original cylindric epithelium about the periphery of the growth has, for the most part, been transformed into flat epithelium,—a usual event after the polyp has hung out of the external os for a while.

Fig. 44. Carcinomatous polyp of the cervical mucosa

Alum-carmin × 60

It is advisable to examine microscopically any mucosal polyp that has attained a certain size and firmness of texture, for, though rarely happening, carcinomatous change in epithelium and gland may develop. The flat epithelia commonly investing mucosal polyps of the cervix, drive wedges and plugs into deep tissues, and then come evolving the well-known alveoli of cancer. Adenocarcinoma has also been observed.

The malignant metamorphosis affects, at first, only the polyp itself, the pedicle remaining unattacked and of a composition entirely benign. Then, removal of the polyp is equivalent to radical obliteration of all cancerous tissue. But the malignant process may extend from the base of the pedicle and involve the mucous membrane of the uterus itself; hence, in examination of such conditions, the pedicle's base demands most particular investigation.

Not every notable stratification of flat epithelia in a polyp is to be interpreted as cancerous in nature, for, when observed at the marginal periphery, it is often an example of epidermidalization only. If we are dealing with a flat epithelium carcinoma, then the carcinomatous alveoli, sometimes with central degeneration (as in the figure), and the irregularities of cell formation are always the essential diagnostic data. In the figure, only the glandular space in the right lower corner is still provided with cervical epithelia of benign character.

Besides the polyps originating in mucous membrane, there are also polyps of fibrous or myomatous tissue, and here also, it is emphatically urged that, in all cases where the least suspicion of the character of such tissue exists, microscopic search for malignant change be instituted. Such metamorphosis consists in either sarcomatous transformation of fibrous tissue or carcinomatous degeneration of the neoplasm, beginning in its mucosal investment, and the technic thereof offers no special difficulties.

Vagina. Vulva

Plate XXIII. Figs. 45 and 46

Plate XXIII

Fig. 45. Carcinoma vaginae

Fig. 46. Condylomata acuminata vulvae

Fig. 45. Carcinoma vaginae

Alum-carmin × 60

Carcinoma in vagina or in vulva is particularly differentiated from other destructive processes, such as ulcers, tuberculosis, lues, by its hardness and its tendency to bleed. Microscopic investigation, then, is notably essential when, as in our specimen, the process is just beginning.

In such case, a typical flat epithelium carcinoma occupies the field, and cancerous alveoli sink from the epithelia of the surface into the depths. Upon the vulva the common type of dermal cancer, namely, the cancroid, develops. At the centers of numerous alveoli are the cancroid pearls, which, on transverse section, appear in sickle-like figures, forming circles or rings.

Fig. 46. Condylomata acuminata vulvae

Alum-carmin × 16

The microscopic diagnosis of vulval carcinoma is difficult only with regard to the possible presence of condylomata acuminata for, in these latter notable proliferation and agglomeration of epithelia also occur which, however, are of secondary development. In condylomata, the primal phenomenon is proliferation of the dermal papillae which bud out, hypertrophy and branch and, synchronously with this progress, there is increase in the strata of epithelia covering the papillae.

Whence, in condyloma of this type there evolve protrusions of connective tissue, and, on transverse section, islands of connective tissue surrounded by epithelia are seen. In a cancer, on the contrary, the epithelial plugs grow primarily in the deeper tissues, so that we have islets of epithelium margined with connective tissue.

The difference becomes plain, if the two specimens are compared. While in Fig. 45 the circumscript epithelial masses lie in connective tissue, the pavement epithelia in Fig. 46 margin, as by a wide and dark broidering, the finger-like processes of stroma into curious forms. Because of their irregularity in direction of growth, the condylomata in the section appear cut longitudinally in part, or obliquely or transversely, but, as they all are surrounded by flat epithelium, there are actually portions where interstitial tissue is observed surrounded by epithelium.

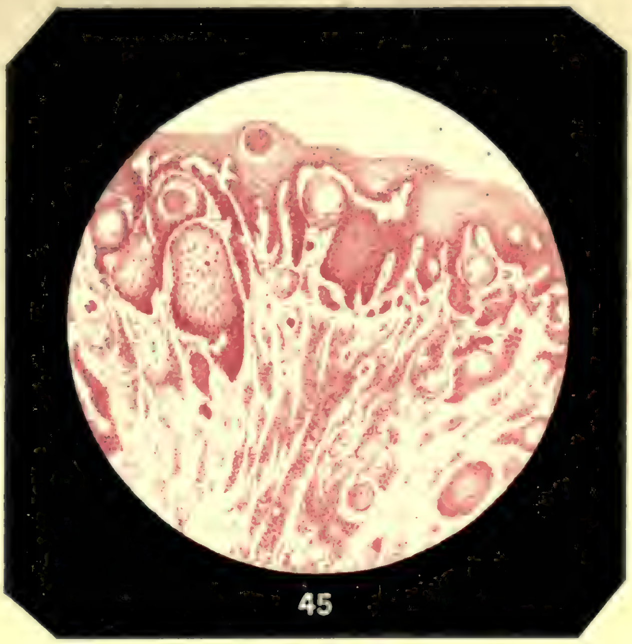

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Fig. 45. Carcinoma vaginae

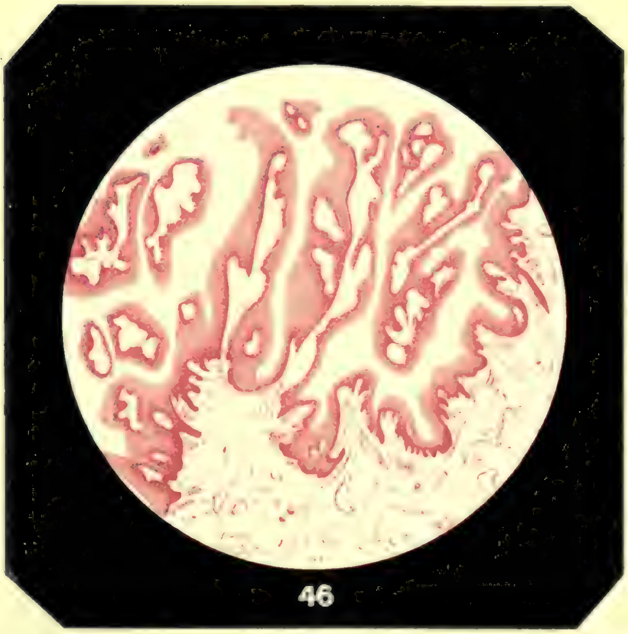

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Fig. 46. Condylomata acuminata vulvae

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Sarcoma Uteri

Plates XXIV and XXV. Figs. 47—50

Plate XXIV

Figs. 47 and 48. Round-cell sarcoma

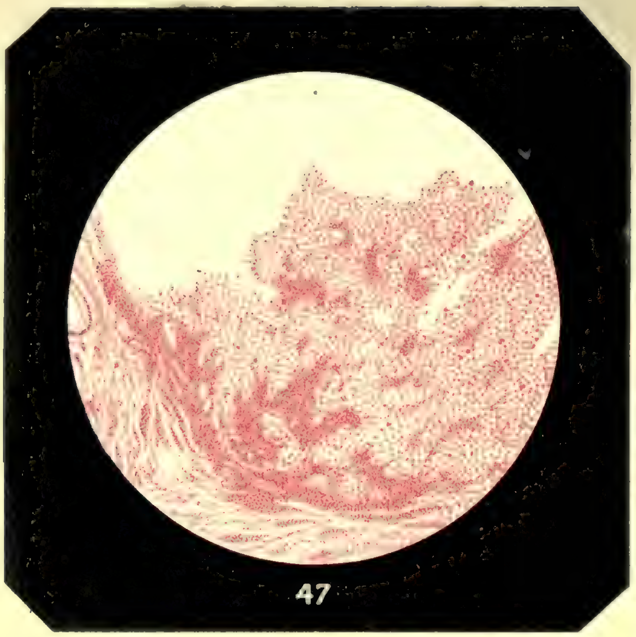

Fig. 47. Round-celled sarcoma

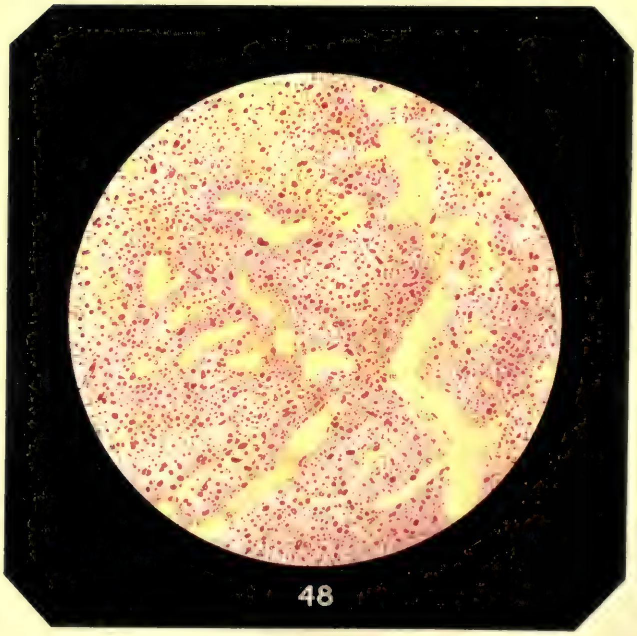

Fig. 48. Round-celled sarcoma

Fig. 47. Round-cell sarcoma

Alum-carmin × 60

Sarcoma, in contrast to cancer, is a neoplasm with origin in connective tissue. In the uterus, therefore, it may develop in the interstitial portion of the mucous membrane: mucosal sarcoma; or in the muscular or the interstitial tissue of the uterine wall: parietal sarcoma.

Mucosal sarcoma presents clinical symptoms similar to those of cancer developing in mucous membrane, and its diagnosis must be established at times from suspected material got by curetment. Parietal sarcoma, on the contrary, pursues a clinical course very like that of a myoma, with thickening of the uterine wall and hemorrhages. In such instance, diagnosis is obtained after separation of the uterus from the patient; sometimes it develops, hitherto unsuspected, on carefuller microscopic consideration of an extirpated myoma.

Of import is the fact that fibroid polyps also, and submucosal myomata flourishing, pediculate, within or without the uterine cavity, are susceptible to sarcomatous degeneration. The observation that fibrous polypi, once removed, again grow, is in many cases probably attributable to a sarcomatous transformation.

Whilst sarcoma may evolve in any part of the uterus, its site of predilection, contrary to that of cancer, is the corpus. Essential microscopic differences in the sarcomatous degenerations of corpus, cervix and portio vaginalis are not known.

In mucosal sarcoma, as here pictured, the stroma cells begin multiplication, develop irregularity of size and shape, and numerous karyokinetic figures appear. The glands become more and more compressed until, over wide areas, epithelial elements are no longer discoverable. In our specimen, the entire visible mucosal territory is already cast to sarcomatous degeneration; marginally, to the left and next the muscle tissues and likewise below, small-celled infiltration is apparent.

Fig. 48. Round-cell sarcoma

Alum-carmin × 84

Microscopically, there are, essentially, three forms or varieties of sarcomata, all of which may occur in mucous membrane and in the uterus: round-celled, giant-celled, spindle-celled.

In the round-celled sarcoma, we have the commonest variety affecting the mucous membrane, though also found in the uterine wall as heaped-up masses between the muscles. There are also small- and large-celled sarcomata of this round-cell type. Frequently, the small-celled growths are difficult to differentiate from normal tissue as the cells are of about the same size. In such case, it is needful to consider particularly the variations and irregularities among the individual cells, characteristic in sarcoma. Moreover, there run always among sarcoma tissues the nutritional vascular channels. These, in the figure (a mucosal sarcoma), appear as yellow, ramifying lines. The varying tinctorial capacities of individual cells are also significant, so that the microscopic aspect of the section is somewhat motley.

Plate XXV

Fig. 49. Round-celled sarcoma

Fig. 50. Spindle-celled sarcoma. Myosarcoma

Fig. 49. Round-celled Sarcoma

Hemalum × 450

It is not always possible to differentiate, with no further to-do, sarcoma from carcinoma by the examination of material got by curet. Sarcoma cells, as they develop, resemble more and more the cellular elements of cancer, and by comparison of the specimen before us with Fig. 32, this is easily realized. It is only under certain conditions that we are able to give a diagnosis of "malignancy," and the decision whether sarcoma or carcinoma be present, is best withheld until (the uterus having been removed) it becomes feasible to make a more careful investigation.

Always, however, the essential thing is recognition of malignancy, when present; and this is gained by comparing the irregular size, form and staining of these cells and nuclei with those of normal tissue as well as by discovery of numerous and atypical mitotic figures. Not infrequently, "giant-cells" are observed,—cells having several nuclei, and those with remarkably moulded, lobate nuclei. Cells of the sort may, too, compose the greater portion of the neoplasm; in which case, it is classified as a giant-celled sarcoma.

Fig. 50. Spindle-celled sarcoma. Myosarcoma

Hemalum × 140

In sarcoma, a characteristic phenomenon and differentiating mark in regard to carcinoma, is the gradual transformation of healthy into sarcomatous tissue. In carcinoma, disregarding advanced cases in which nothing is seen but cancer cells, we observe the sharp-drawn demarcation between cancer alveoli and glands and the surrounding connective tissue. With sarcoma, on the contrary, normal cells change or pass by imperceptible transition into abnormal cell and tissue.

These pictures of gradual change, the lack of sharp delimitation; such factors render diagnosis extremely difficult at times. Hence, it is necessary in such case to compare most carefully the individual cells, and these, finally, will establish their variability and malignant character.

In myosarcoma, the transition of cellular elements is particularly distinct. In the specimen (lower left region) the incipient, remarkable increase in size of the muscle cells, the increase in nuclei, the irregularity of form evidence its malignant character. Further, the muscle elements lie in normal arrangement and the fibers are interwoven as in healthy tissue.

Besides these genuine myosarcomata, there may also be seen sarcomatous, round-celled masses developing among normal muscle tissues. These present the ordinary aspect of round-cell sarcoma and, contrary to rule, are sharply delimited from the surrounding muscle tissue.

Among the numerous forms of sarcoma, its combination with cancer, where carcinomatous glands are environed with sarcomatously degenerate connective tissue, demands especial mention.

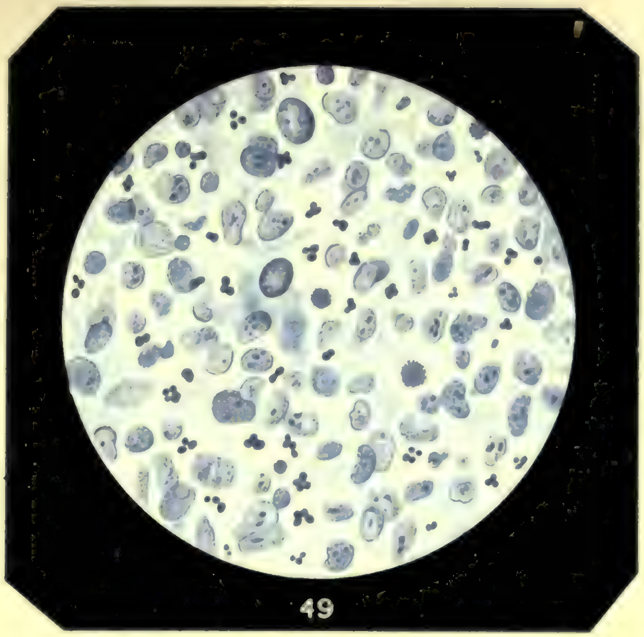

Fig. 49. Round-cell sarcoma

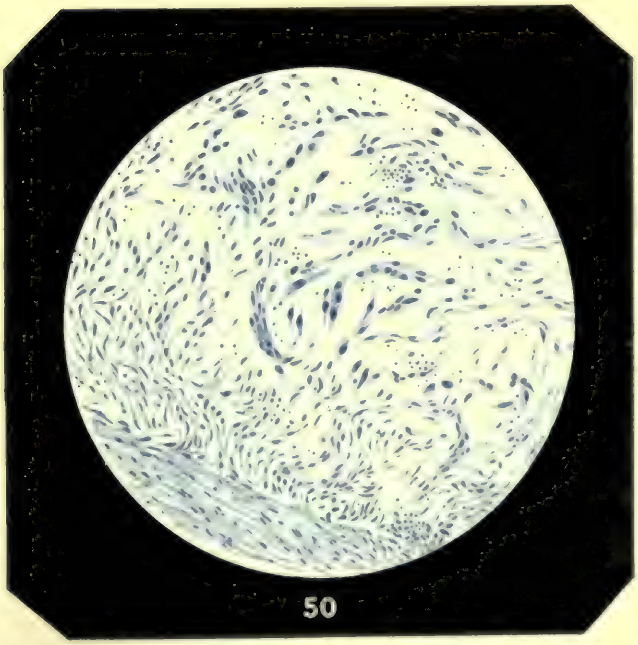

Fig. 50. Spindle-cell sarcoma. Myosarcoma

Catarrhal Secretions

Plate XXVI. Figs. 51 and 52

Plate XXVI

Fig. 51. Vaginal catarrh

Fig. 52. Urethritis gonorrhoica

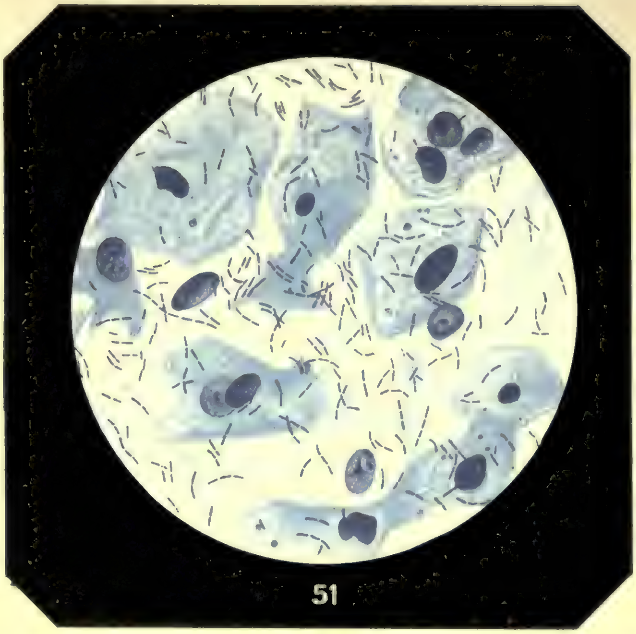

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Fig. 51. Vaginal catarrh

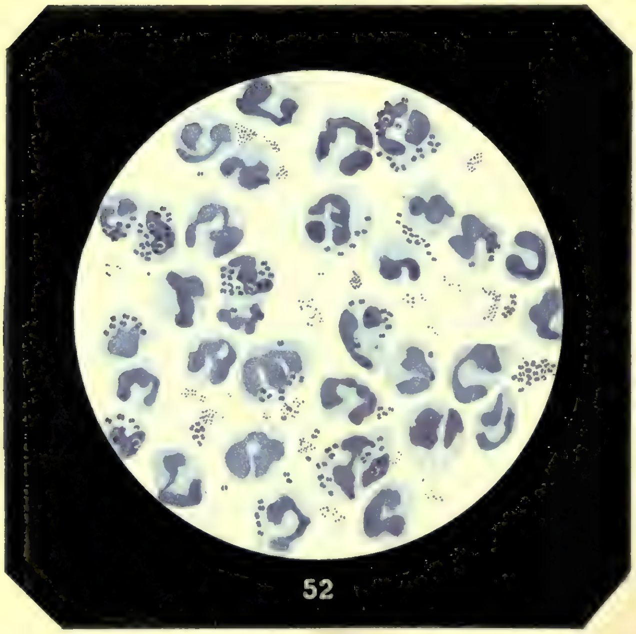

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Fig. 52. Urethritis gonorrhoica

Fig. 51. Vaginal catarrh

Methylen blue. Oil-immersion. × 880

The normal secretion of the vagina contains desquamated flat epithelia as the corpuscular elements of its mucous or serous fluid component. These epithelia, viewed microscopically, are large polygonal cells, often very irregular in form. They have a large round or oval nucleus, centrally located, and staining well. As in the right lower part of the specimen, the cells frequently remain coalesced; in other areas, because of too thick a smear, they lie upon one another, so that a single cell seems to possess several nuclei.

With absolutely no morbid conditions present, various species of bacteria are found in the vagina. Most common are the large bacilli depicted in the figure, either separate or in long chains, and irregularly distributed. They are innocuous.

Among infectious microbes, the gonococcus is of the most import in gynecology. Very rarely, true diphtheria bacilli are found. Staphylo- or streptococci are commonest in connection with the lying-in period.

Fig. 52. Urethritis gonorrhoica

Methylen blue. Oil-immersion. × 880

Where there is a gonococcal infection, the secretion is almost diagnosable as specific because of its purulency, the smear, therefore, containing pus corpuscles. These are easily differentiated from flat epithelia as they are smaller, more nearly circular in contour, and have polymorphous nuclei of the most varying shape and sometimes, apparently, two in a cell.

Purulent secretion may also have other bacteria as etiologic factors; in which case, the bacteria concerned will be found between or outside of the cells, while gonococci, on the contrary, prefer residence within the cell itself, and, occasionally, even within the nucleus.

Gonococci are large diplococci, deeply stained with methylen blue. The two component and slightly bent cocci lie with their concavities in apposition, so that the pair have the appearance of semmel seeds or of French biscuits. Ordinarily, they are seen assembled in large groups.

In the vagina, the gonococcus is difficultly found, allied as it commonly is, with numerous other varieties of bacterial life. The urethra, however, which is almost invariably affected, presents the gonococcus in clearer aspect. In the specimen of gonococcal catarrh from the urethra depicted in Fig. 52, the intracellular location of the microbe is particularly evident. When gonococci lie within the nucleus, they are typically surrounded by a clear marginal zone. The masses of smaller cocci present in the smear are not of gonococcal ancestry.

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